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EDITA IUSSU SOCIETATUM RADIOLOGICARUM
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VOL. 41 MARCH 1954 FASC. 3

PULMONARY CIRCULATION TIME

A Densometric Study

by

Björn Nordenström

A procedure for temporarily occluding one of the pulmonary arteries in dog or in man has previously been described (2). It is effected with the aid of an ordinary heart catheter having a rubber balloon affixed to its tip. When this instrument has been passed by way of a peripheral vein into the pulmonary artery selected, the bloodflow is stopped by filling the balloon with a fluid contrast medium.

Momentary differences apart, the minute volume is the same in the systemic and pulmonary circulations (4, 11). This would seem to be unaffected by unilateral occlusion of the pulmonary artery, for it has proved possible to keep the artery occluded for up to two hours without signs of circulatory complications (2).

Sudden stoppage of the circulation through one lung — such as after pneumonectomy or during temporary occlusion of a pulmonary artery — means that as much blood will flow through the contralateral lung per unit time as formerly passed through both lungs combined. If there is anything to prevent this, the condition induced will soon give rise to grave circulatory disturbances. In order that the minute volume in the pulmonary circulation shall remain constant when one lung assumes the function of both, concomitant haemodynamic changes must occur in that lung. This would be impossible unless the blood volume circulating in the lung or the circulation time through the lung, or both these factors, were altered.

The present investigation is an experimental study in dogs of the

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From the Roentgen Department (Director: Docent B. Holmgren), Sabbatsbergs Sjukhus, Stockholm, Sweden.

effect of temporary occlusion of a pulmonary artery on the circulation time through the contralateral lung.

Roentgenologic methods have previously been adopted for studies of the pulmonary circulation time, the passage of a dose of opaque medium through the heart and pulmonary vessels being observed roentgeno-cinematographically (10, 1, 5, 9). A procedure combining angiography and roentgenkymography has also been proposed (3). However, such techniques necessitate the injection of comparatively large doses of contrast medium. But the contrast media used hitherto have had physical characteristics differing from those of blood (6), and therefore their circulation times provide only relative values for the circulation times of blood. Accordingly such roentgendiagnostic methods were considered inadequate for these studies of the effect of occlusion of one pulmonary artery in dogs.

A technique was therefore evolved in which an electrokymograph was used to determine the transit time through the pulmonary circulation of small amounts of contrast medium, before and after occlusion of one pulmonary artery.

Equipment

The electrokymograph (The Standard Direct-writing Electrokymograph, made by Elema-Järnh, Stockholm, and designed by K. BERGLUND) has certain special features that will be described briefly:

Record distortion due to external influences is diminished by a balanced circuit, whereby the need for filtration is reduced to about one tenth and the effects of roentgen source variations due to line fluctuations are almost eliminated.

The arrangement of the various components is shown in fig. 1. P_1 is a photomultiplier tube behind the subject and indicates the subject's absorption plus roentgen source fluctuations due to line voltage variations. Phototube P_2 receives directly the beam from the roentgen tube. Current I_2 from this tube will therefore vary directly as the roentgen intensity. Hence the difference between currents I_1 and I_2 from the two phototubes will be proportional to the intensity of the roentgen beam after it has passed through the subject and vary only with any absorptive changes, *e. g.* those caused by heartbeats. By means of this balanced bridge circuit the roentgen source variations due to line voltage fluctuations were made to cancel out.

The filter is designed to give the highest possible degree of electrokymographic information with the lowest possible noise level from any standard roentgen installation. A full-wave rectified roentgen ray (50

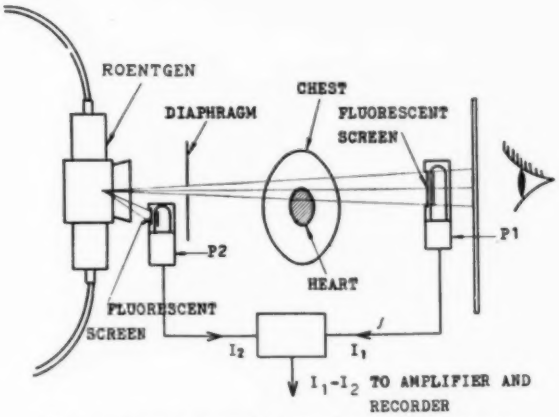

Fig. 1. The balanced electrokymograph circuit.
Phototube P_1 behind the subject and phototube P_2 between the subject and the roentgen source produce currents I_1 and I_2 directly proportional to the intensity of the rays impinging on the phototube targets. I_1 and I_2 are in antiphase when fed to the amplifier.

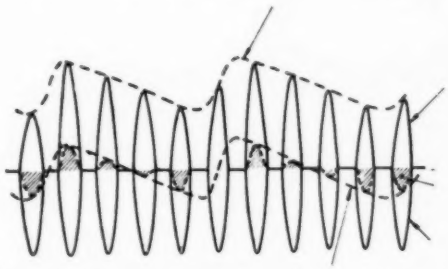

Fig. 2. Roentgen source intensity variations are eliminated by antiphase coupling.

cycle line) consists of pulses with a rectified frequency of 100 cycles per second. The highest intelligence frequency these pulses can carry is 50 cycles per second. Since 'noise' is proportional to the band width, the filter is designed to cut off at 50 cycles per second.

To make possible the recording of very slow rates of contrast medium disappearance, a D. C.-coupled amplifier is used. This introduces practically no delay for the low-frequency component of the intelligence signal. A very steep front might be delayed by two or three hundredths of a second — the response to a step function is exemplified in fig. 4. Errors in the circulation time measurements due to instrument inaccuracies are thus so small as to be negligible.

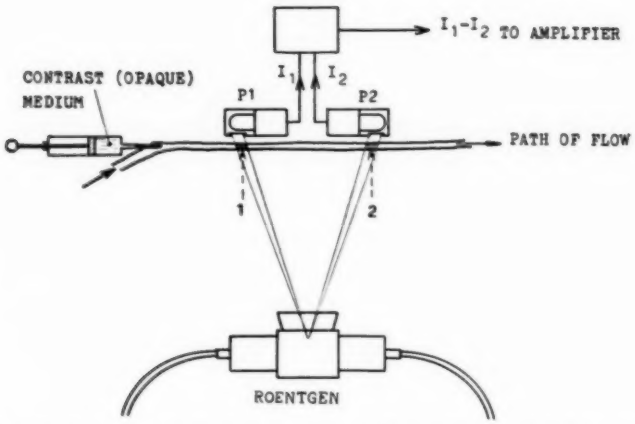

Fig. 3. Phototubes P_1 and P_2 are placed over different points of a vessel. After a contrast medium injection, the radiation hitting P_1 is first reduced (upstroke) followed by that hitting P_2 (downstroke). As in the arrangement in fig. 1, the balanced coupling eliminates roentgen source intensity variations.

The circulation time for the contrast medium was measured with the phototubes arranged as in fig. 3. The slits of P_1 and P_2 faced the vessel, and the circuit was such that an upstroke was recorded when contrast medium passed P_1 and a downstroke when it passed P_2.

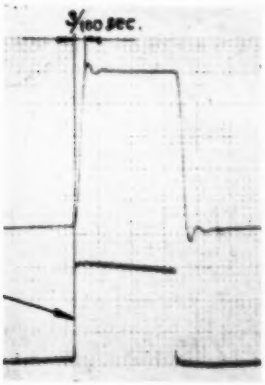

Fig. 4. Use of a DC amplifier introduces no appreciable time lag. A step function gives a lag of 0.02—0.03 seconds.

The aperture slits of the phototubes measured 6 by 26 mm. The area of these slits could be reduced by means of movable brass sleeves (fig. 5). By adjusting the aperture, it was possible to compensate roughly for those intensity variations of the total flux impinging on the phototube targets which were caused by density differences in the tissues interposed between the vessel and the apertures of P_1 and P_2. Full compensation was achieved by electrical means, *i. e.* through adjusting the dynode voltage of either photomultiplier tube.

Electrocardiograms (lead II) were traced at the same time as roentgen absorption changes — *i. e.* densograms — were recorded.

The *roentgen radiation* was generated by a

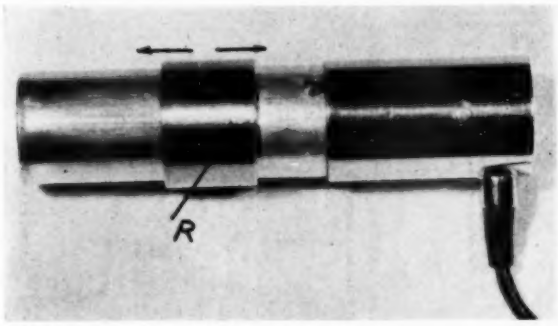

Fig. 5. The width of the phototube's aperture slit can be varied with a brass sleeve (R) slipped over its shield assembly.

standard 6-valve machine, the densograms generally being recorded at 3 mA and 70 kV.

Heart catheters. Ordinary single-bore heart catheters of size 6 or 7 were used for occlusion of one of the pulmonary arteries. The orifice of the catheter was plugged and a new hole pierced 2 or 3 cm from the tip. A thin-walled rubber balloon was slipped over this hole and lashed on securely with fine nylon thread. To the opposite end of the catheter was attached a piece of rubber tubing with a spring clip for opening or closing

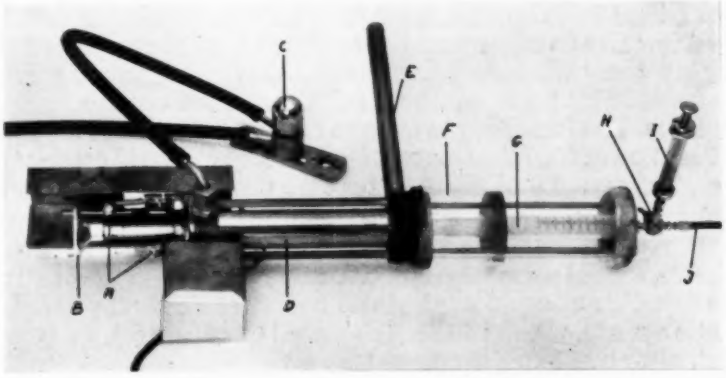

Fig. 6. Construction of automatic syringe.

A. Two contactor rings for microswitches. B. Pusher ram knob which actuates microswitches. B. Pusher ram knob which actuates microswitches. C. Air line valve. D. Air cylinder. E. Rod for clamping. F. Protective end guard. G. Glass syringe. H. Three-way cock. I. Syringe for filling heart catheter with contrast medium. J. Heart catheter.

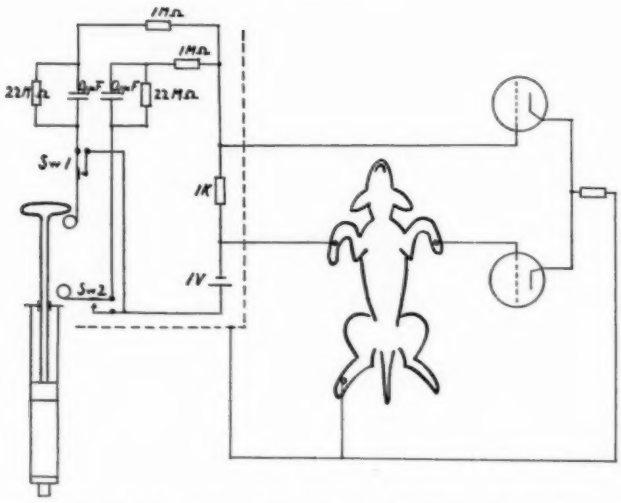

Fig. 7. Circuit for indicating start and termination of automatic contrast medium injection.

the passage to the catheter as required. A solution of iodopyracet thirty-five per cent (w/v) was the contrast medium used to expand the balloon.

Contrast medium was introduced into the vessels by means of a size 10 single-bore catheter having its orifice plugged and with two diametrically opposed lateral holes about one cm from the tip. The latter feature was provided in order to counteract the tendency for the catheter to retract which may occur when a contrast medium is ejected from a single hole under considerable pressure. It was felt, too, that opaque medium so injected would be less liable to become dispersed than after an injection in the direction of the blood current from the tip orifice of an unmodified catheter. The capacity of the catheter bore was 2.2 ml.

Syringes. In a preliminary series of experiments the contrast medium was manually injected with an ordinary 5 ml syringe. As this was thought undesirable, special steps were taken to achieve the controlled and reproducible injection of equal amounts at uniform rates and pressures. An automatic syringe, which has been described elsewhere (8), was therefore adopted, after slight modifications (fig. 6.)

A Luer-Lok glass syringe having a capacity of 10 ml was fitted in the holder of the syringe stand. A three-way cock was interposed between the socket of the heart catheter and the syringe, whereby it became possible to fill the heart catheter with contrast medium from a 5 ml syringe. The contrast dose in the heart catheter was then expelled into the

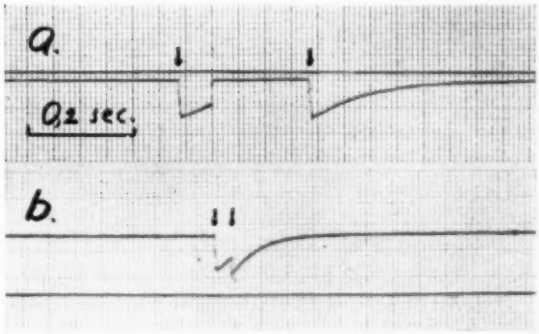

Fig. 8. Marks indicating beginning and termination of injection: a. slow injection (0.25 seconds), b. rapid injection (0.04 seconds).

blood stream by means of an equal volume of physiological saline from the automatic syringe. This was done to reduce the volume of fluid injected at each injection of contrast medium. The ram of the air cylinder on the syringe stand was arranged to push home the plunger of the glass syringe when a valve in the compressed air line to the cylinder was opened. The pressure of the air supply was regulated by means of a reducing valve with a manometer on the compressed air tank. A pressure of 15 kg per square cm was generally adopted, and this made it possible to inject 2.2 ml (capacity of heart catheter) of contrast medium in 0.1 to 0.2 seconds.

The duration of the injection was registered as follows. The shaft of the ram carried two slidable microswitches, Sw_1 and Sw_2, so mounted that the ram actuated Sw_1 at the beginning of the stroke and Sw_2 at its termination. When Sw_1 or Sw_2 made contact a brief pulse-like signal was applied across a resistor of 1 KΩ. A slow injection gave a voltage of the appearance shown in fig. 8 a, a fast injection one as in fig. 8 b. As appears in fig. 7, this signal voltage was connected in series with the ecg voltage.

Fluids injected. Contrast medium: iodopyracet (Umbradil, Astra) 70 %.

Anaesthetic: pentobarbital sodium (Nembutal, Abbott) in alcoholic solution.

Anticoagulant: Heparin (Vitrum) in 5 % solution (1 ml = 5,000 I. E. = 50 mg standard heparin).

Technique

1. The animals were anaesthetized with pentobarbital administered intraperitoneally in a dosage of 0.5 ml per kg body weight. Occasionally

this was supplemented with one or more intravenous pentobarbital doses of 0.5 ml. 0.5 ml of heparin per 10 kg body weight in physiological saline was injected intravenously.

2. The animals were placed in the dorsal position on a trochoscope. Under fluoroscopic inspection the balloon catheter was inserted into a femoral vein and passed via the right heart into one of the pulmonary arteries which was occluded. Under similar control, the stout single-bore catheter was inserted into a peripheral vein and passed either to the right auricle or to the trunk of the pulmonary artery.

3. The animals were placed halfway between the supine and right-side-down positions. Phototube P_1 was positioned over the pulmonary artery close to the bifurcation of the trunk, and P_2 over the left auricle. By slightly shifting the positions of P_1 and P_2 and adjusting their apertures by means of the brass sleeves, the operator sought to obtain constant densograms with minimal variations despite high degrees of amplification.

4. The automatic syringe was filled with 2.2 ml of physiologic saline after the microswitches had been set to indicate that volume. Through the side-arm of the three-way cock the heart catheter was filled with iodopyracet 70 %. The densogram recorder was then started, the connection to the syringe opened and air admitted. The physiologic saline from the automatic syringe thus expelled the contrast medium from the heart catheter.

5. After contrast medium injections made while a pulmonary artery was occluded, the occlusion was removed by aspiration of the contrast medium contained in the balloon fitted to the heart catheter. New densograms were then made with fresh doses of iodopyracet 70 %.

The Densographic Record

When contrast medium flowed past phototube P_1 (pulmonary artery) the rays reaching it were attenuated. This made the curve being traced rise to a higher level. At the same time there was a rise in the amplitude of the pulsations of the pulmonary arteries owing to the greater density differences obtaining when the pulsating vessel contained contrast medium. When contrast medium passed below the aperture of P_2 (left auricle) the densographic tracing fell to a lower level because of increased roentgen absorption. At the same time the amplitude of the auricular contractions increased owing to greater density differences between the various contraction phases.

The graph paper used for the recordings had a time scale imprinted on it, whereby the pulmonary circulation time could be computed as

follows. A point on the electrocardiogram halfway between the marks indicating the beginning and the end of the injection was taken as the first reference point. The densographic minimum during left auricular response was taken as the second reference point. The latter point was found by drawing a line through the midpoints of the deflections synchronous with the heartbeats in the densogram, the lowest point on the line thus described being the second reference point. These two points were sufficient to determine the relative pulmonary circulation time. Nevertheless phototube P_1 was kept as an extra reference point as a check on the passage of contrast medium through the pulmonary artery.

Materials

Experiments were altogether made on 21 dogs weighing from 12 to 24 kg. The first 13 experiments constituted a preliminary series carried out while the technique was being developed. The pulmonary circulation time was determined in 8 experiments, and in 6 of these the effect of unilateral pulmonary artery occlusion was studied.

Results

Experiment no. 5 is illustrated in fig. 9. 2.2 ml of iodopyracet 70 % was injected into the right auricle by means of the automatic syringe. Phototube P_1 was placed over the left pulmonary artery close to its origin in the arterial trunk. Phototube P_2 was placed over the left auricle close to the entry of the left pulmonary vein.

The passage of contrast medium below the aperture of P_1 (pulmonary artery) was accompanied by an irregular deviation upwards in the densogram. On the other hand, owing to the reversed polarity of P_2, contrast medium passing through the left auricle caused the curve to fall to a lower level. Simultaneously the amplitude of the curve variations synchronous with the auricular contractions increased.

Curves a, b and c are densograms recorded while the right pulmonary artery was occluded. Curve d was recorded immediately after the lumen of the right pulmonary artery had been reopened and curve f 15 minutes later. Curve h was obtained during renewed occlusion of the right pulmonary artery.

The time which elapsed from the injection of the contrast medium to the appearance in the densogram of the left auricular response was shorter when a pulmonary artery was occluded than when the blood could circulate freely through both lungs.

A fluctuation of high frequency will be observed in the right half of curves b to e. It was caused by respiratory distortion of the densograms.

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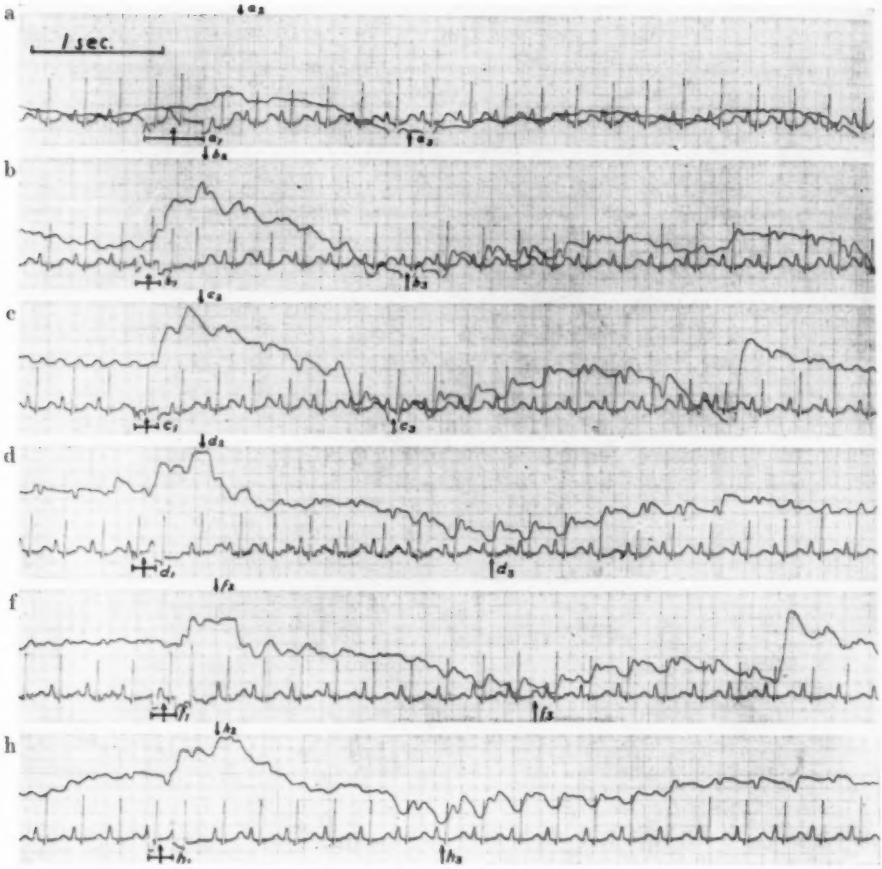

Fig. 9. Experiment no. 5: 2.2 ml of iodopyracet 70 % was injected into the right auricle (a_1—h_1). The curves deviated upwards when contrast medium passed phototube P_1 over the pulmonary artery (a_2—h_2) and downwards when it passed phototube P_2 over the left auricle (a_3—h_3). Curves a, b and c were recorded with the right pulmonary artery occluded, curve d immediately after removal of the occlusion, curve f 15 minutes later, and curve h shortly after renewed occlusion of the artery. Contrast medium travelled from the right auricle to the left in shorter time when one pulmonary artery was occluded than when circulation through both lungs was free.

Fig. 10 illustrates densograms b to f of experiment no. 8 where, unlike the other experiments, the transit time for the passage of the contrast medium from the pulmonary artery to the ascending aorta was measured. With the animal rotated 45° to the left from the supine position, 2.8

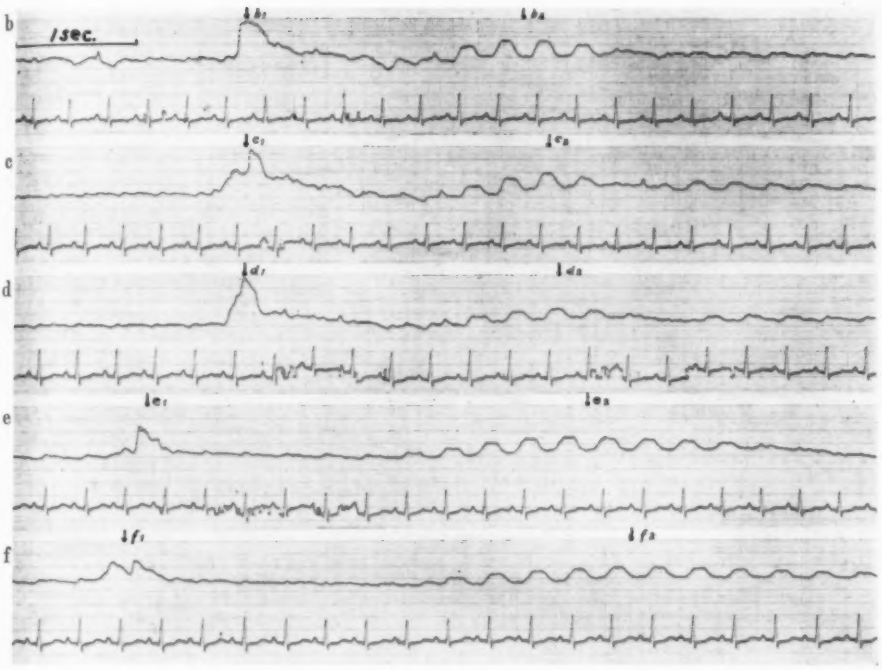

Fig. 10. Experiment no. 8: Phototube P_1 was placed over the pulmonary artery and the ascending aorta simultaneously, the two vessels being projected superimposed on one another. Contrast medium passing the pulmonary artery produced peaks b_1—f_1 and the ascending aorta (one more beneath P_1) a second maximum (b_2—f_2). Curves b, c and d were recorded with the left pulmonary artery occluded, curve e immediately after removal of the occlusion, and curve f 10 minutes later. When one branch of the pulmonary artery was occluded, contrast medium required less time for travelling from the pulmonary artery to the ascending aorta than when circulation could take place freely through both lungs.

ml of iodopyracet 70 % was manually injected into the trunk of the pulmonary artery by means of a single-bore size 10 catheter having a transversely perforated tip. The first densographic maximum represented the passage of contrast medium through the pulmonary artery. The second series of increased pulsations accompanied by elevation of the densogram ('the aortic response') represented the passage of contrast medium through the ascending aorta. In this particular case the same phototube, P_1, was used for reference points over the vessels by virtue of the fact that the aorta and the pulmonary artery were projected superimposed on one another. As the animal's position precluded an unobscured projec-

Tab. 1

Experiment	Weight of dog, kg.	Injection (ml of 70 per cent iodopyracet)	Injection time	Right auricle — Pulm. artery — Left auricle — Ascending aorta (Systole)	Heart rate per 15 sec.	Pulm. circulation
1 a	15	2.3		2.3	49	Free
b		»		2.1	48	»
c		»		2.2	44	»
d		»		2.9	43	»
e		»		3.1	42	»
2 a	15	2.2	0.16	3.5	39	Free
b		»	0.15	3.5	41	»
c		»	0.16	2.2	39	Immediately after occl. of left p. a.
d		»	0.16	2.4	40	5 min. after occl. of left p. a.
3 a	16	2.0		3.2	34	Free
b		»		3.1	33	»
4 a	15	2.8	0.22	2.1	50	Left p. a. occluded.
b		»	»	2.1	50	— » —
c		»	»	1.7	50	— » —
d		»	»	2.8	50	Free
5 a	15	2.2	0.46	1.8	54	Right p. a. occluded
b		»	0.18	2.0	55	— » —
c		»	0.18	1.9	53	— » —
d		»	0.14	2.7	53	Free. Immediately after release of occl.
e		»	0.18	2.6	53	Free 5 min.
f		»	0.16	2.6	53	» 10 min.
g		»	0.18	2.8	54	» 15 min.
h		»	0.18	2.1	51	Immediately after occl. of right p. a.
6 a	12	2.2	0.09	1.9	45	Right p. a. occluded
b		»	0.10	1.9	42	— » —
c		»	0.10	2.4	42	Free. Immediately after release of occl.
d		»	0.16	2.4	43	Free 10 min.
e		»	0.16	2.4	44	» 15 min.

Tab. 1 (Cont.)

Experiment	Weight of dog, kg.	Injection (ml of 70 per cent iodopyracet)	Injection time	Right auricle	Pulm. artery	Left auricle	Ascending aorta	Heart rate per 15 sec.	Pulm. circulation
			S — e — c — o — n — d — s						
7 a	12	2.2	0.18		2.5			37	Free.
b		»	0.12		2.6			38	Free.
c		»	0.12		1.9			38	Right p. a. occluded 2 min.
d		»	0.10		1.9			38	Right p. a. occluded 10 min.
8 a	19	2.8			2.3			51	Left. p. a. occluded
b		»			2.2			48	— » —
c		»			2.4			50	— » —
d		»			2.5			48	— » —
e		»			3.5			48	Free. Immediately after release of occl.
f		»			4.0			46	Free. 10 min.

tion of the left auricle, phototube P_2 was placed over the right inferior pulmonary vein. Densograms b to d were recorded with the left pulmonary artery occluded, curve e immediately after removal of the occlusion and curve f 10 minutes later. The interval between the maxima was shorter for curves recorded with occlusion of a pulmonary artery than for curves recorded without such occlusion.

A synopsis of the results obtained in all the experiments will be found in table 1.

In all experiments except no. 1 and 3, densograms were recorded during free circulation as well as during occlusion of either pulmonary artery. In these 6 experiments the contrast medium took less time to circulate from the first to the second reference point when the pulmonary artery of one side was occluded than when the circulation through both lungs was unobstructed.

The circulation times and heart rates obtained will be found in fig. 11. No direct association between these two factors could be traced in this series of experiments.

Discussion

Movement of the tissues underneath the phototubes might give rise to distortion of the densograms. This actually happened in some cases.

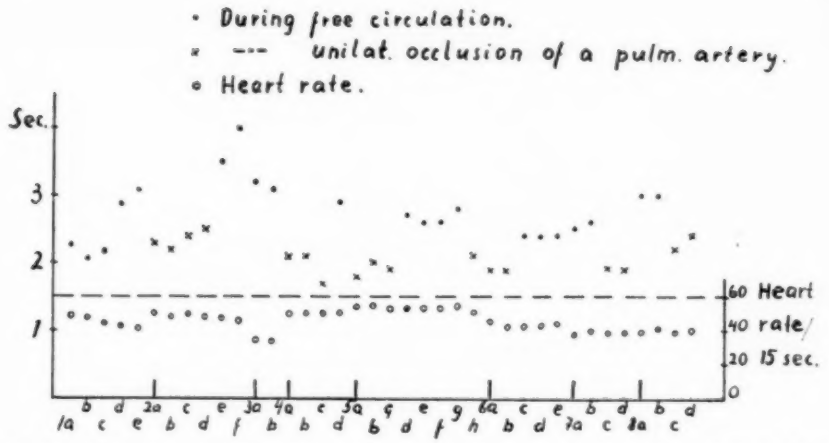
• During free circulation.
× --- unilat. occlusion of a pulm. artery.
○ Heart rate.
Sec.
3
2
1
60 Heart
40 rate/
20 15 sec.
0
1a b c d e 2a b c d e 3a b c d e 4a b c d e 5a b c d e f g 6a b c d e 7a b c d e

Fig. 11. Transit times (taken from table 1) through the pulmonary circulation and heart rates.

The shortening effect on transit time through the pulmonary circulation of pulmonary artery occlusion clearly shown. No direct association between transit time and heart rate can be perceived.

Whenever this occurred either or both the phototubes were wholly or partly displaced from the projection area over the vessel or heart cavity concerned during some phase of the respiratory cycle. A direct check on this could be made by means of fluoroscopic observation during the contrast medium injections. Furthermore, positional changes were associated with characteristic deviations of the densograms. Examples of such deviations are the typical distortions of the right part of curves 5 b—e. In this experiment distortion took place after the contrast medium had completed its transit through the pulmonary circulation, and therefore the distortion lacked significance for the evaluation of the densograms. The cause of such respiratory distortion is obscure; a central respiratory reflex due to the contrast medium is one possibility.

In every animal the transit time for the contrast medium through the pulmonary circulation was shorter when one lung was cut out of the system by occlusion of its artery than when there was free passage through both lungs. This relative change of the circulation time of the contrast medium may be explained by a corresponding change of the circulation time for blood. Such an explanation seems reasonable in view of the fact that the minute volume passing the pulmonary circulation must be maintained even when one lung is put out of action through occlusion of its artery.

The right and the left lung of dogs differ negligibly in weight (7). Consequently it has been assumed that the same amount of blood normally

passes through the right and the left lung in the same animal. If so, occlusion of a pulmonary artery would halve the circulation time, provided that no more than a changed circulation time is required to compensate for the loss of the circulation through one lung. However, a glance at fig. 9 will show that the transit time from the pulmonary artery to the left auricle was apparently not reduced to half its former value after occlusion of the contralateral pulmonary artery. Hence it seems reasonable to suppose that the second means whereby the pulmonary circulation could be compensated — a change in the volume of blood circulating through the lung — contributed to the maintenance of the minute volume. In these circumstances the pulmonary circulation must have adapted itself to unilateral occlusion of a pulmonary artery both by shortening of the circulation time through the lung and by increasing the blood volume passing the lung per unit time.

SUMMARY

A densometric procedure, developed for studying the circulation time for small volumes of contrast medium injected into the vascular system, is described.

The technique has been tested in a series of experiments in dogs, the aim being to ascertain the effect of occlusion of a pulmonary artery on the transit time through the pulmonary circulation. The transit time through the pulmonary circulation was shorter when one pulmonary artery was occluded than when there was unobstructed circulation through both lungs. This phenomenon would seem to constitute an appropriate compensatory haemodynamical change since it is essential that the minute volume is maintained even when one lung is removed from the circulation. The experiments provided indirect evidence suggesting that the pulmonary circulation adapts itself to occlusion of the pulmonary artery to one lung also through augmentation of the blood volume circulating through the contralateral lung.

ZUSAMMENFASSUNG

Eine densometrische Methode für das Studium der Zirkulationszeit kleiner Mengen von Kontrastflüssigkeit, welche in das Gefäss-system injiziert werden, wird beschrieben. Als Densometer wurde ein Elektrokymograph angewendet.

Die Methode wurde in einer Versuchsserie an Hunden ausgeführt. Hierbei versuchte man, die Wirkung einer einseitigen Absperrung der Lungenarterie auf die Zirkulationszeit durch den kleinen Kreislauf zu bestimmen. Bei den Versuchen hat sich gezeigt, dass die Zirkulationszeit durch den kleinen Kreislauf bei Absperrung einer Lungenarterie kürzer wird als bei unbehinderter Zirkulation durch beide Lungen. Es scheint, dass es sich hier um eine (passende) kompensatorische Veränderung der Hämodynamik handelt um das Minutenvolumen aufrecht zu erhalten, auch wenn die Zirkulation durch eine Lunge abgesperrt wird. Die Versuche haben auch indirekte Anhaltspunkte dafür gegeben, dass die Anpassung des kleinen Kreislaufes bei Absperrung der einen Lungenarterie auch durch eine Vermehrung des zirkulierenden Blutvolumens in der anderen, nicht abgesperrten Lunge, erfolgt.

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RÉSUMÉ

L'auteur décrit une méthode densimétrique mise au point pour étudier le temps de circulation de petites quantités de produit de contraste injectées dans le système vasculaire. Un électrokymographe a servi de densimètre.

Cette technique a été essayée au cours d'une série d'expériences sur des chiens, dont le but était de déterminer l'effet de l'occlusion d'une artère pulmonaire sur la durée du transit à travers la circulation pulmonaire. La durée du transit à travers la circulation pulmonaire s'est montrée plus courte quand une artère pulmonaire était obstruée que quand la circulation était libre à travers les deux poumons. Ce phénomène semble être une modification compensatrice favorable de l'hémodynamique, étant donné qu'il est essentiel que le débit par minute soit maintenu même quand un poumon est exclu de la circulation. Ces expériences ont fourni des arguments indirects qui font penser que l'augmentation du volume sanguin circulant dans le poumon controlatéral contribue à l'adaptation de la circulation pulmonaire à l'occlusion de l'artère pulmonaire d'un poumon.

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GASTRIC MOTIVE FUNCTION

WITH PARTICULAR REFERENCE TO THE ACTIVITY OF THE CONDUCTING SYSTEM IN THE STOMACH

by

Bengt Lilja

Gastric roentgenology is comprehensively treated in the literature, interest being centered primarily on the mucosa under physiologic and pathologic conditions. The function of the muscular coat has also been studied, and disturbances of motility have been demonstrated, particularly in stenosis. An adequate explanation of the originating mechanism of certain important pathologic roentgen findings, however, is still lacking.

In 1953, the writer demonstrated a characteristic disturbance of gastric motivity in cases of severe ulceration in or near the incisura angularis. In such cases a pouch-like dilatation of the sinus ventriculi (Forssell's sinus), frequently called pars pylorica in the American literature, is observed, with impairment of motivity. Arrhythmia occurs in the form of a dissociation in the motivity of the vertical part of the stomach in relation to that of the horizontal part. This arrhythmia implies that the normally continuous motive co-operation between the parts is interrupted at the incisura angularis. The writer has suggested that this phenomenon be called gastric block, and has compared it with the arrhythmic phenomenon in the heart. For the occurrence of such a gastric block a motive centre for the transverse stomach situated at the incisura angularis, must be assumed. In severe ulceration the function of this centre is abolished. The assumption of such a motive centre agrees well also with observations on the physiologic manifestations of the stomach's motivity.

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In ulceration of the incisura angularis with gastric block, it is frequently possible to demonstrate an abnormal contraction of the canalis ('the pyloric antrum' in the American literature). A permanent contraction of the canalis often appears in these cases. In pronounced cases the appearances resemble those in pyloric stenosis in children. At times, however, there is a non-characteristic functional impairment of the canalis and occasionally also a rather widely patent pylorus. Prepyloric contractions have been observed before in ulcer of the incisura angularis, and have been variously interpreted. No satisfactory explanation of their origin has been given.

Gastric block of the incisura angularis accordingly, implies an impairment of the normal rhythm of gastric motility. Through destruction of the motive centre in the incisura angularis, a local muscular insufficiency in the sinus arises and frequently also an impaired tonus in the wall of the canalis.

Experimental physiologic investigations have shown that various parts of the gastric muscular coat have different characteristics. Thus, there is a considerably greater tonus of the lesser curvature than of the greater curvature. The inclination to rhythmic contractions as well as the electric irritability is greater on the lesser curvature, and greatest near the cardia. ALVAREZ ascribed significance to these graded differences in rhythmicity, irritability, tonicity and latency in the regulation of peristalsis. He also expressed the opinion that peristaltic waves have their origin at the site where the musculature is most rhythmic and sensitive. He stated further, "It may be that, ordinarily, the highly rhythmic region on the lesser curvature next to the cardia serves as a sort of pacemaker for the body of the stomach, with a similar region near the incisura for waves going over the pars pylorica". Under pathologic conditions these varying characteristics in the musculature appear to make possible the occurrence of characteristic disturbances of motility in the various parts of the stomach.

With consideration to both the physiologic and roentgenologic observations mentioned, investigation seems merited as to whether ulcers in the longitudinal stomach (fundus + corpus) might also cause disturbances in the gastric motivity extending even beyond the actual site of the ulcer.

In the current literature it is stated that gastric ulcers may cause a local shrinkage of tissue. A 'schneckenförmige Einrollung' of the lesser curvature is also mentioned, and it is stated that a contraction of the longitudinal musculature may be a contributary cause. A real shrinkage may possibly occur in cases of severe ulceration. Deformation of the stomach in other ways may certainly occur in fixation of the ulcer and formation of adhesions in the surrounding area. But such

'shrinkage' has also been observed on the roentgen examination of small ulcers, although operation may prove the stomach to be free from adhesions and infiltration in the region of the ulcer very moderate.

For a long time changes have been demonstrated roentgenologically on the greater curvature in cases of ulcer on the lesser curvature. In the early days of roentgenology, it was even believed that a corresponding contraction on the greater curvature, a 'spasm', was a sign of ulceration. The spasm may alter in site and extent in different cases, and no acceptable explanation of its changing character seems to exist.

So-called gastritis characterized in the roentgenogram by a coarse and irregular folding of the mucosa, has been studied. However, no universal explanation of its origin and clinical significance has been reached. On the contrary, there has been an increasing lack of agreement between the roentgenologic, histologic and gastroscopic observations. The abnormal folding that usually accompanies an ulcer frequently affects only a circumscribed area of the stomach. It does not usually appear in the immediate vicinity of the ulcer, but rather is most marked on the greater curvature. Generally also it includes only a limited part of the greater curvature.

From these short remarks it is evident that the origin of common and important roentgenologic signs is still questionable.

In ulceration on the lesser curvature of the longitudinal stomach, a regularly recurring contraction may be observed on the greater curvature (Figs. 4—7). This contraction has a characteristic appearance. It includes a greater or lesser area of the greater curvature of the longitudinal stomach descending from the level of ulceration with a typical extension. The contraction appears as an inward bulging of the contour of the greater curvature in the affected section, thus decreasing the width of the lumen of the stomach. If the stomach is filled with a large quantity of heavy contrast medium, the inward bulging may temporarily disappear, but with slight and moderate filling it remains visible.

In addition, within the contracted area in the lower part of the body of the stomach, a radiating fan-like folding is seen. The picture is typical and constant when the ulcer is situated on the lesser curvature side of the longitudinal stomach (Figs. 4 c, 5 c). If the folding is to be visualized, however, the quantity of contrast medium must again not be too large. The folding usually appears most clearly when the patient is lying. In the upright position, the heavy contrast medium collects in the lower part of the stomach, stretching and distending it so that the radial folding is obliterated (Figs. 4, 5).

Belonging also to the typical picture described of ulceration of the longitudinal stomach, is an increased serration of the contour of the greater curvature, with deep and frequent folds having the same delimi-

tation as mentioned in the case of a local contraction. In other words, a sign is observed that was, at least formerly, regarded as an indication of local gastritis. However, modern writers issue a warning against hasty conclusions regarding increased gastric folding as an indication of organic gastritis because experience has shown that gastritis frequently cannot be histologically or gastroscopically demonstrated in conjunction with this finding.

All these roentgenographic changes described in the lower part of the longitudinal stomach are characteristic both in situation and form as well as being regularly recurrent in different patients. Attention was therefore concentrated upon the possibility that there might be an underlying anatomic cause. We find in studies in the anatomic literature that the inner muscular layer has a radial distribution in the lower part of the longitudinal stomach which will correspond to the roentgen finding (Fig. 2). Indeed, the roentgenologic changes described may be explained if they are correlated with the anatomic distribution of the inner muscular layer. There is nothing corresponding to this inner muscular layer in other sections of the digestive tract.

The following description of the muscular structure of the stomach is taken from the excellent anatomic work on the stomach by FORSSELL (1913).

The tunica muscularis of the stomach consists of an outer layer with longitudinal muscular fibers and inside this of a layer with circular fibers. Together, these two layers of longitudinal and circular musculature correspond to the structure of the muscle wall in the entire digestive tract. In addition, in the stomach, there is the aforementioned inner muscular layer of primarily oblique muscular fibers with a special structure. This inner layer may be rather easily differentiated macroscopically. According to Forssell, it serves as a support for the stomach. The suspensory apparatus is also said to consist of a medial longitudinal fasciculus of the superficial muscular layer along the lesser curvature and the ligamenta ventriculi on both sides of the transverse stomach.

The inner oblique muscular layer (Fig. 1) consists of a superior part, which forms concentric rings around the fornix or fundus, with fibers which blend with the circular layer more laterally in the fornix. The inferior part, which is included in Forssell's suspensory sling, forms rather wide bands which continue along the lesser curvature at some distance from the 'midline' of the curvature, with one band in the anterior wall of the stomach and one in the posterior. Superiorly, these muscular bands in the anterior and posterior walls of the stomach join in the angle between the oesophagus and the fornix. These strong, band-like bundles of muscular fibers have a triangular distribution in the muscular coat anteriorly and posteriorly, and are said to be the strongest

muscle bundles in the stomach. They give off medial branches in the direction of the lesser curvature. Laterally, the muscular fibers from the bands are inserted, in part, in the circular muscular layer in the anterior and posterior walls of the stomach, along a line sited somewhat medially to the midline between the lesser curvature and the greater curvature. Lateral to this line of insertion, fibers of the inner muscular layer are intimately related to the circular muscular layer and follow its fibers, freely anastomosing with some of these as far as the greater curvature. In addition, fibers of the inner muscular layer are inserted in the submucosa. Inferiorly, the inner muscular layer terminates at the level of the incisura angularis near the ligamenta ventriculi in the transverse stomach, being absent in the transverse stomach.

The fibers in the oblique inner layer are said to have a special anatomic structure, deviating from that of the fibers in the adjacent circular layer (FORSSELL). They are finer and exhibit anastomoses but rarely. It has been demonstrated anatomically that the inner muscular layer remains a differentiated muscle in all degrees of contraction. The straight course of the inner muscular layer even in contraction shows motivity independent of the circular layer (Fig. 3).

An explanation of the changes in the inferior part of the ulcerated longitudinal stomach may be obtained by considering the function of the inner muscular layer. In cases of ulceration of the lesser curvature the muscular coat is stimulated to contract. A local inward bulging of the greater curvature at the lower part of the longitudinal stomach is then obtained, and a radial folding spreads in the form of a fan from the ulcer, corresponding to the anatomic distribution of the inner muscular layer in this region (Fig. 2). The 'gastritis' picture as well, with the locally increased serration of the greater curvature, may be explained through an increased folding caused by contraction of the muscular coat with a shortening of the wall. It is possible that the mucosa through its muscularis mucosae actively takes part. The anatomic statement that the fibers of the inner muscular layer are inserted not only in the circular muscular layer but also in the submucosa supports this possibility. But it must be the contraction of the inner muscular layer that is the causative factor. This is the only explanation of the constant limitation of the phenomenon to the extension of the inner muscular layer.

The roentgenologic signs in the inferior part of the longitudinal stomach, which accompany the niche on the lesser curvature, form a triad with 1) inward bulging on the greater curvature with constriction of the lumen, 2) folding radiating from the ulcer, and 3) increased 'gastritis-like' serrations of the contour of the greater curvature. This triad may, without doubt, be ascribed to a common cause, *i. e.* a spastic

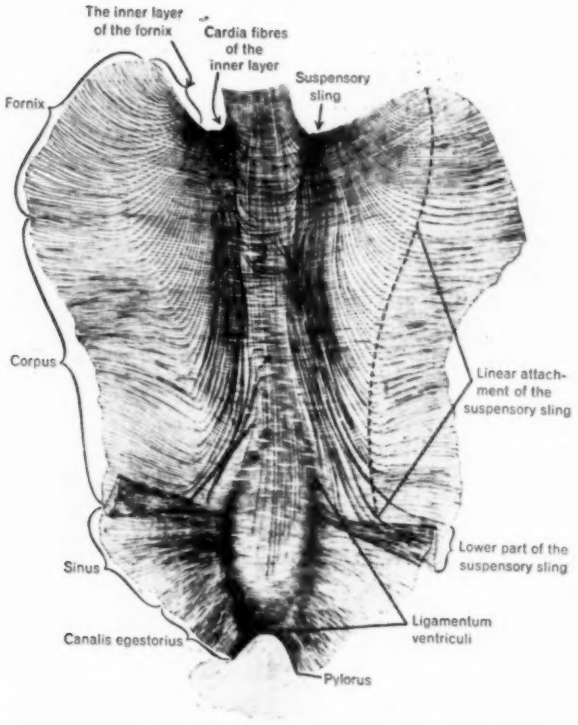


Fig. 1. The inside of the stomach showing the extension of the inner muscular layer. (FORSSELL.)

contraction of the inner muscular layer beneath the ulcer. One prerequisite, however, is that the ulcer has involved this muscular layer. Because of its distribution, sometimes in the anterior, but usually in the posterior wall near the lesser curvature, however, this is almost always the case.

The fan-like distribution of the inner muscular layer in the lower part of the longitudinal stomach presents special reasons for attributing to this layer definitive significance in the roentgenologic changes arising in ulceration of the lesser curvature of the longitudinal stomach.

Other striking changes caused by the contraction of the inner muscular layer also occur in the stomach. But the difficulties in drawing conclusions concerning the decisive influence of the inner muscular layer in this connection are somewhat greater, due to the considerable normal variability of the stomach. It is well known that the length of the

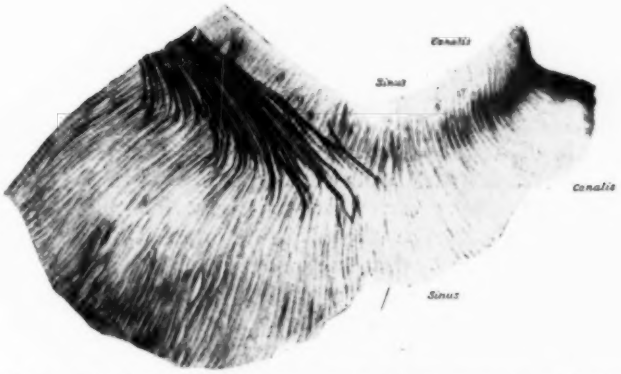


Fig. 2. The inside of the lower part of the stomach with the inner muscular layer. (FORSSELL.)

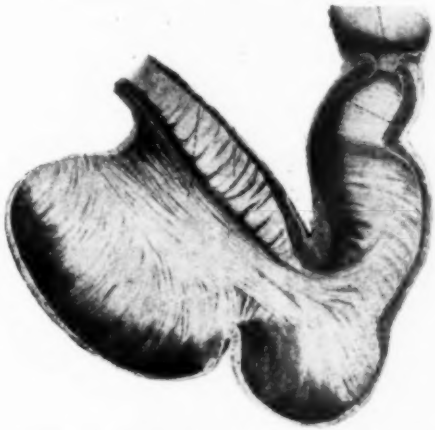


Fig. 3. The inner muscular layer of the stomach. (After Cunningham from FORSSELL's book.)

stomach as well as its tonus vary considerably from patient to patient. The earlier roentgenologic literature in particular treats in detail with the great differences in the appearance, length and tonus of the stomach in different bodily constitutions. The extreme variants occur, on the one hand, in the thin asthenic type of individual in which the body of the stomach is elongated and on the other hand, in the pyknic type in which the stomach resembles a bull's horn and is situated in the upper part of the abdomen. In addition, the stomach is foreshortened in an ordinary roentgenogram. It is also well known that the stomach closes

around its contents, contracting with a small quantity of contrast medium and becoming larger with more abundant filling.

Because of the varying situation and shape of the stomach in different patients, there are apparent changes in form due to its projection in roentgenography. If the stomach is situated in the upper part of the abdomen and is of a more sagittal and less vertical shape than usual, it will be foreshortened in the conventional frontal projection. As in all roentgenography, ordinary errors due to distortion must be considered (cf. the writer's book on the site of the corpus pineale, in which such errors in skull roentgenography are reviewed and estimated).

If an ulcer affects the inner muscular layer in its superior course, a contraction should include a major portion of this muscular layer. Such a contraction should then appear as a shortening of the longitudinal stomach, a decrease in its width, and an increased folding of the mucosa in the greater part of the extension of the inner muscular layer. And this is indeed what is observed. When the ulceration is high, the entire body of the stomach is observed to be shortened, especially along the lesser curvature. Furthermore, the longitudinal stomach usually has a decreased width as well (Figs. 10, 12). The result of the shortening is that the transverse stomach will be more or less drawn up and the distance between the cardia and the pylorus thus shortened, rounding off the incisura angularis (Figs. 4, 7). Moreover, a limited ring-like contraction is sometimes observed on the greater curvature, at the level of the ulcer. This no doubt corresponds to the horizontal course of the muscular fibers in the inner muscular layer (Fig. 5).

These characteristic changes consisting of shortening of the longitudinal stomach and drawing up of the transverse stomach with rounding off of the incisura angularis must not be confused with normal variations of the stomach in subjects with different physical constitutions. Nor must apparent changes in form due to the roentgenographic projection influence the estimation. On the other hand, the fact that the inherent motivity of the stomach has previously been misinterpreted may possibly be explained by these circumstances.

The roentgenologic appearances described apply to ulceration of the stomach with a lesion of the inner muscular layer. It is only natural in a biologic series that borderline cases in which it is difficult to differentiate between a change and a normal variant, occur. For this reason a knowledge of the normal variability is necessary. But the diagnosis of ulceration is facilitated to a great degree through collation of the aforementioned secondary signs in the roentgenologic triad. They indicate the probable situation of the ulcer and thus facilitate demonstration of the niche.

In cases in which only one ulcer involves the inner muscular layer,

the diagnosis may be easy and the roentgenologic signs typical. But appearances presenting more difficulty in interpretation are not rare. Two niches may occur in the longitudinal stomach (Fig. 14), of which perhaps only one catches the eye if the investigation is not carried out methodically. Ulcers situated high up in the stomach have long had the reputation of being difficult to diagnose. Renewed study of earlier roentgenograms from this department has shown that such ulcers were sometimes overlooked before the secondary changes discussed herein were fully exploited for the localization of the ulcer. It has been observed also that ulcers in this situation now occur more frequently than previously.

After the healing of ulcers which have caused a contraction of the inner muscular layer, the changes due to the contraction usually remain. In that case, only the secondary changes without any niche, are observed, (Fig. 5 b), and we must be satisfied with establishing the signs existing of a contraction of the inner muscular layer within a particular area.

In addition to the characteristic secondary changes noted in ulceration of the lower part of the longitudinal stomach, signs of a contraction of the inner muscular layer above the ulcer may sometimes also be observed, although further ulceration at a somewhat higher level cannot be demonstrated. For this, there are various theoretic explanations: 1) that, in fact, an additional higher ulcer is present, 2) that such an ulcer previously present has healed, 3) that a change exists in the mucosa, which has not advanced as far as ulceration but has caused an irritation of the inner muscular layer at this point, 4) that contraction may also originate in a region above an ulcer, 5) that a contraction of the muscular layer precedes the appearance of an ulcer, and finally, 6) that a contraction may occur even without the formation of an ulcer. The present material presented by the writer, however, does not appear to admit of more than the two first-mentioned possibilities; *i. e.* that an ulcer exists at a higher level or that such an ulcer has healed with residual contraction affecting the inner muscular layer also in the upper part of the stomach.

Inasmuch as a contraction of the inner muscular layer in the longitudinal stomach is rather common even when no ulcer can be demonstrated, it is quite possible that such a contraction of the inner muscular layer may occur without an ulcer and possibly predispose to ulcer formation. Concerning this possibility, as previously stated, the present material affords no information. A continued investigation of this question might be possible with the help of gastroscopy. In this case, attention should be concentrated upon a study of the region near the cardia, but with the present type of gastroscope this area is not yet accessible.

Complicated appearances are also obtained if, in addition to involve-

a. b.

c.

Fig. 4 (Case 1).

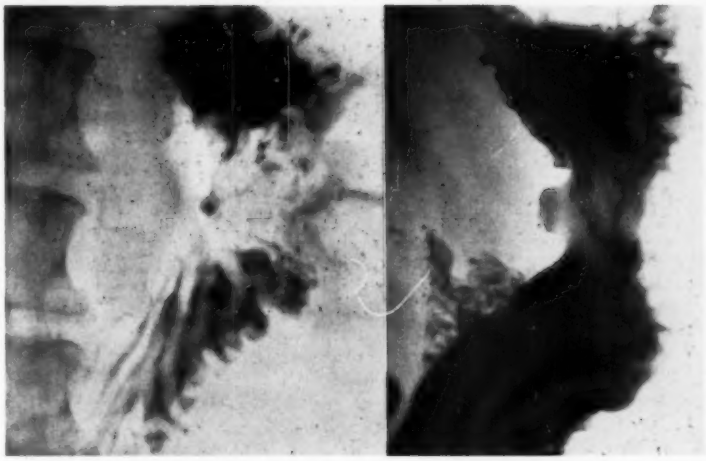
a. Oct. 30th, 1950. Appreciable ulcer crater with shortening and decreased width of the longitudinal stomach and rounding off of the incisura angularis.

b. Inward bulging in the lower part of the longitudinal stomach.

c. Dec. 11th, 1950. Small residue of the ulcer and a fan-like folding in lower part of the longitudinal stomach.

ment of the inner muscular layer in the longitudinal stomach, the motive centre in the incisura angularis is inhibited by ulcer formation. This may occur if two separate ulcers exist, but also if a single ulcer crater is situated at the point of transition between the longitudinal and the transverse stomach. Typical signs of ulceration of the longitudinal stomach may then be observed, in addition to an effect upon the transverse stomach, evidenced by a dilatation and disturbed motivity of the sinus (Fig. 14). Moreover, in this case, there may be a change in the tonus of the gastric wall in the canalis. The roentgen appearances in these cases are rather complex.

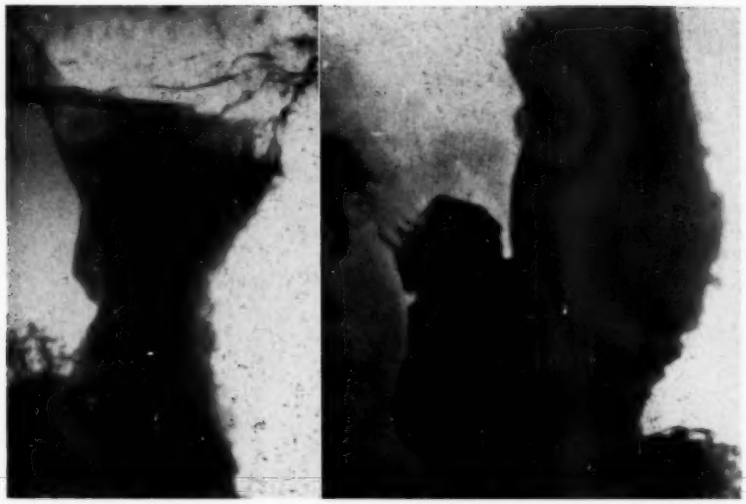
a. b.



c. d.

Fig. 5 (Case 2).

a. June, 17th, 1946. Ulcer crater with shortened lesser curvature and contraction of the greater curvature. Lower part of the stomach is distended by contrast medium.
b. July, 23rd, 1946. No ulcer crater demonstrable. Radial folding visible in lower part of the longitudinal stomach.
c. Sept. 3rd, 1947. Recurrence of the ulcer. Fan-like folding in lower part of the longitudinal stomach.
d. Jan. 7th, 1948. Further recurrence of the ulcer. The longitudinal stomach is shortened and decreased in width. The transverse stomach is drawn up; folding increased.



a. b.

Fig. 6 (Case 3).

a. Dec. 23rd, 1947. Almond-sized ulcer crater in the longitudinal stomach with shortening and decreased width, as well as increased folding on the greater curvature.

b. June, 19th, 1950. Bean-sized recurrence of the ulcer. Increased folding observed on the greater curvature side of the longitudinal stomach, notwithstanding that the stomach is appreciably distended by contrast medium.

The following series of eleven cases is presented to illustrate the roentgenologic signs in ulceration of varying situation and degree of severity in the longitudinal stomach. Only typical ulcer cases with a niche have been included. Some of the patients (five cases) had gross ulcers that were operatively treated. In these the roentgenologic observations could be compared with information from the operative reports and histologic examinations. The latter were carried out in the Pathologic Institution at Lund (AHLSTRÖM). In one case a post-mortem examination was performed without previous operation. In the other five cases the condition did not lead to operation, the changes being less severe or the patient's age and general condition such that operation was not considered desirable.

Case 1. (Fig. 4.) L. H., aged 71, had complained for about one month of epigastric pain. In Fig. 4 a an ulcer crater of considerable size may be seen on the posterior wall near the lesser curvature. An appreciable contraction of the inner muscular layer is shown by a rounding off of the incisura angularis, arising through a shortening of the longitudinal stomach with drawing up of the transverse stomach. Moreover, there is an inward bulging of the greater curvature in the lower part of the longitudinal stomach together with an increased radial folding.

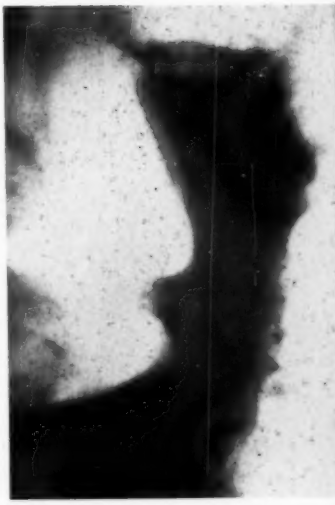


Fig. 7.

Fig. 8 a.

8 b.

8 c.

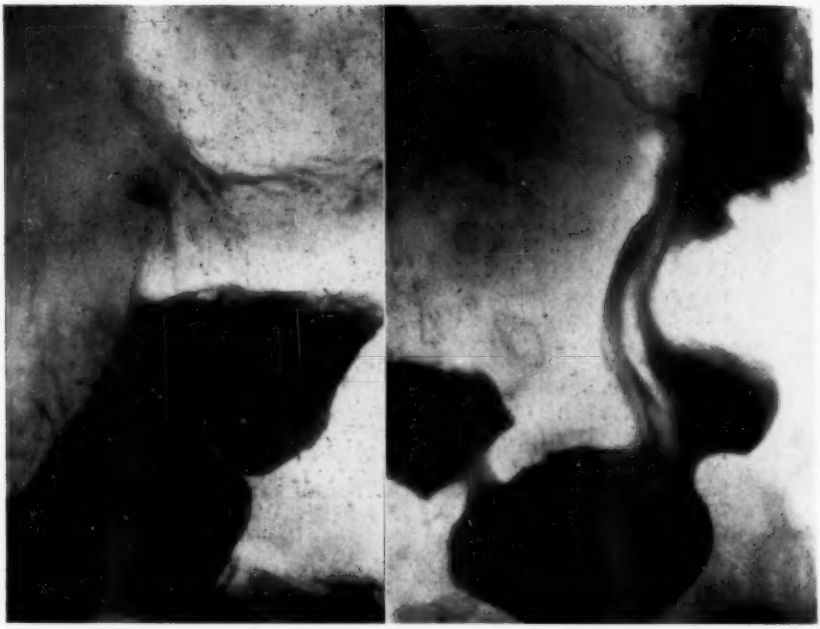
Fig. 7 (Case 4). Feb. 17th, 1949. Niche in longitudinal stomach, which is shortened and has decreased in width. The incisura angularis is rounded off. Increased folding of the contour of the greater curvature.

Fig. 8 (Case 5).

a. Aug. 19th, 1944. Ulcer craters in longitudinal stomach, which is shortened and decreased in width in the lower part.

b. Dec. 10th, 1948. Constant fold penetrating deep into the greater curvature. Greater shortening of the lesser than the greater curvature has given rise to a pouch-like formation in the lower part of the longitudinal stomach. (Cf. Fig. 3.)

c. March, 28th, 1950. Hourglass-shaped stomach with ulceration on the lesser curvature.



a. b.

Fig. 9 (Case 6).

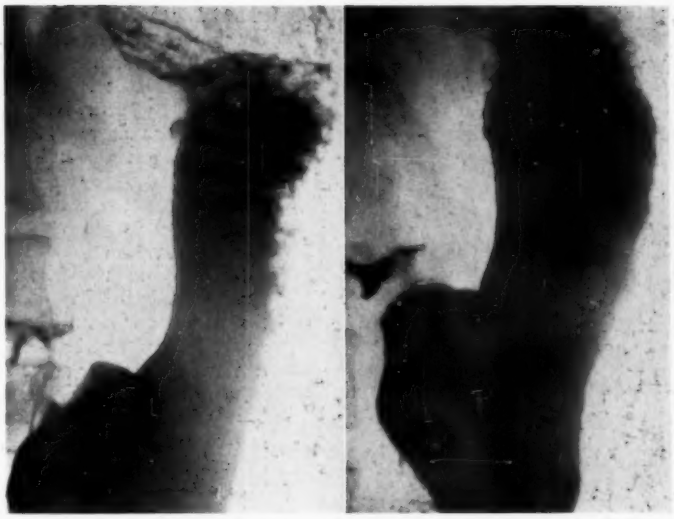
a. Jan. 11th, 1952. Hourglass-like stomach with ulceration high on the severely contracted lesser curvature. Pouch-like formation in the lower part of longitudinal stomach, above the fold.

b. Jan. 11th, 1952. In the film exposed with the patient prone, a coarse longitudinal fold may be seen, continuing below the inward bulging on the greater curvature. (Cf. Fig. 3.)

Case 2. (Fig. 5.) J. A. J., aged 62, with typical ulcer symptoms since 1941, had undergone roentgen examination several times during the period. The figure shows an ulcer crater in the longitudinal stomach in various stages of development. In Fig. 5 b the ulcer crater appears temporarily healed following five weeks' medical treatment. Signs of a contraction of the inner muscular layer may be inferred from a shortening of the longitudinal stomach, its decreased width, a drawing up of the transverse stomach, and a radial folding in the lower part of the longitudinal stomach.

At *operation* in 1949, an ulcer about 2.5 cm in diameter was found on the lesser curvature above the incisura angularis, with sclerosis of the serosa. *Histologic examination* showed the ulcer to be of a markedly callous character. Under a necrotic superficial layer, cicatricial connective tissue was observed, interrupting the musculature in the vicinity of the ulcer. The fibrous transformation extended out to the surface of the serosa.

Case 3. (Fig. 6.) G. A., aged 45, gave a history of gastric symptoms starting in 1946. The ulcer crater had caused a contraction of the inner muscular layer. This



a. b.

Fig. 10 (Case 7).

a. Dec. 11th, 1952. Ulcer crater below the cardia with contraction of longitudinal stomach inferior to the level of the ulcer, and increased folding on the greater curvature.
b. Dec. 11th, 1952. Slight inward bulging of the lesser curvature in the lower part of longitudinal stomach.

is shown by a shortening of the longitudinal stomach, which also has a decreased width in the lower part and an increased folding of the contour of the greater curvature. The ulcer healed after treatment, but recurred three times. The last recurrence was in June 1950.

At *operation* (June, 1950) an area of infiltration on the lesser curvature was discovered. The preparation revealed an ulcer about one cm in diameter. *Histologic examination* showed that the ulcer niche was surrounded by rather callous scar tissue. The base of the ulcer had undergone superficial necrosis with abundant leucocytic infiltration. The underlying fibrous tissue could be seen infiltrating the entire gastric wall and radiating out into the surrounding omentum.

Case 4. (Fig. 7.) G. K., aged 66, had had periodic epigastric pain and occasional vomiting for many years. A niche in the longitudinal stomach was first demonstrated in 1946. Since that time the patient had had repeated recurrences. Operative treatment was not considered possible because of the patient's age and poor general condition. The figure shows that the niche was accompanied by a contraction of the inner muscular layer.

Case 5. (Fig. 8.) N. E. N., aged 53, had been admitted to hospital several times since 1944 for ulcer symptoms with pain and vomiting. As early as 1944 a large area of ulceration was observed on the lesser curvature of the longitudinal stomach, which

Fig. 11 (Case 8). Aug. 15th, 1952. Ulcer below the cardia with contraction of the entire body of the stomach and increased folding on the greater curvature.

showed marked contraction of its lower part. On examination in 1948 a deep fold was demonstrated on the greater curvature. This had further developed by 1950, giving the stomach an hourglass shape. The contraction of the inner muscular layer appeared to have drawn in the contour of the greater curvature, causing the characteristic appearance.

At *operation* in March, 1950 an ulcer high on the lesser curvature side, surrounded by appreciable infiltration, was found. The preparation showed an ulcer about 2 cm in diameter on the lesser curvature. *Histologic examination* disclosed that the base of the ulcer was covered with fibrin crusta with abundant leucocytic infiltration. The gastric wall at that site exhibited complete callous transformation and coarse streaks of connective tissue could be seen radiating out into the surrounding fatty tissue. The fibrous tissue forming the base of the ulcer was densely infiltrated with inflammatory cells.

Case 6. (Fig. 9.) A. N., aged 67, gave a history of haematemesis in 1928, and occasional gastric symptoms from that time.

The figure shows the appearances in 1952. Through the severe contraction of the inner muscular layer on the lesser curvature aspect, the stomach has assumed an hourglass shape. Above the deep fold on the greater curvature, a pouch-like formation may be seen in the lower part of the longitudinal stomach with the patient in the upright position (Fig. 9 a). In the prone position (Fig. 9 b) the broad longitudinal grooves descend along the lesser curvature even past the deep fold in the greater curvature. (Cf. Fig. 3.) Thus, the inner muscular layer probably also extends below the hourglass constriction.

Case 7. (Fig. 10.) F. S., aged 35, with a history of melena following periodic gastric symptoms. An ulcer high up below the cardia had caused a contraction of the entire longitudinal stomach, which also exhibited an increased folding on the greater curvature. Fig. 10 b shows also a slight inward bulging of the lower part of the greater curvature side, corresponding to the extension of the inner muscular layer.

Case 8. (Fig. 11.) F. S., aged 48, had had pain suggestive of perforation following several days of sub-acute epigastric symptoms, and underwent operation. A juxta-

Fig. 12.

Fig. 13.

Fig. 12 (Case 9). Jan. 20th, 1951. Ulcer crater high on the lesser curvature. The longitudinal stomach shows decreased length and width and a rounded off incisura angularis. Unusually pronounced folding in the fornix.

Fig. 13 (Case 10). Aug. 28th, 1952. Marked contraction of entire longitudinal stomach with ulcer crater below the cardia. There is pronounced radial folding in the fornix.

pyloric ulcer was found, with a quill-sized perforation into the abdominal cavity. Gastrorrhaphy was performed.

However, after the operation the patient was not asymptomatic and gastric discomfort continued. Renewed roentgen examination showed an ulcer below the cardia and a contraction of the entire body of the stomach, which also showed an appreciable folding of the contour of the greater curvature.

Case 9. (Fig. 12.) E. L., aged 55, gave a history of periodic gastric distress of the ulcer type since 1942, when a small niche sited in the canalis was demonstrated for the first time. In 1947 the patient vomited blood. In January 1951 an ulcer crater was observed high up in the longitudinal stomach, which showed an appreciable contraction of the lower part as well as a greatly increased folding in the fornix. This corresponded to the extension of the superior portion of the inner muscular layer. The unusually coarse folding in the fornix, according to the histologic examination, may not have been caused by inflammatory changes.

At *operation* in July, 1951, an ulcer was found high up on the lesser curvature. The preparation showed an ulcer about 1.5 cm in diameter on the lesser curvature. *Histologic examination* revealed that the ulcer had a rather deep base, with a necrotic, pyic coat, under which lay an abundantly cellular granulation tissue extending with

Fig. 14 (Case 11). May, 16th, 1952. Small ulcers high on the lesser curvature and above the incisura angularis. The entire longitudinal stomach is contracted with an increased folding. Somewhat dilated sinus; contracted canalis.

fibrous streaks a considerable distance down into the muscularis. In addition, there were large areas of fibrous scar tissue radiating out into the surrounding submucosal connective tissue. The surrounding antral mucosa showed pronounced gastritic changes with diffuse and focal plasma cell infiltrations. There were no indications of malignancy. At the superior border of the resection the mucosa was of the fundus type and only slight inflammatory irritation was observed in that region.

Case 10. (Fig. 13.) O. P., aged 67, had had gastric haemorrhages in 1937 and 1938 and again in July, 1952. On the 4th August, 1952, an ulcer crater the size of a large hazel-nut was demonstrated below the cardia. The crater had decreased in size on re-examination on the 28th August when a very marked shortening of the longitudinal stomach was observed. This observation was difficult to evaluate, however, both because of the patient's marked spinal deformity and because the ulcer might well have been penetrating and adherent to the surrounding tissues. This case has been included to show the unusually severe contraction of the upper portion of the inner muscular layer in the fornix, which exhibited a pronounced radial folding. The patient was kept in the Surgical Department in the hope that his general condition would improve sufficiently to permit of an operation. However, after a sudden deterioration in his condition, he died on the 8th October, 1952.

Post-mortem examination showed an ulcer the size of a thum-tip on the lesser curvature, which penetrated into the liver. The wall between the stomach and the omental bursa was thin as paper but not perforated. There was extensive arteriosclerosis of the coronary vessels of the heart.

Case 11. (Fig. 14.) F. H., aged 58, with gastric symptoms beginning in 1943, when a small ulcer was demonstrated above the incisura angularis. The patient vomited blood in December, 1948. The ulcer recurred in May, 1952. A small ulcer crater was observed at that time above the incisura angularis. A somewhat dilated sinus and a contraction of the canalis indicated an effect upon the motive centre in the incisura angularis. However, another small ulcer crater is also observed. This ulcer, lying high up on the lesser curvature with an appreciably increased folding in the longitudinal stomach, had been overlooked at the previous roentgen examination and the subsequent operation.

At *operation* in June, 1952, an infiltration, about 3 cm in diameter, was found on the lesser curvature approximately at the incisura angularis. It was noted that the wall of the pyloric region also felt unusually thick and firm. The preparation showed

an ulcer, the size of the tip of a little finger, on the lesser curvature and, in addition, a thickening of the gastric wall close to the pylorus. *Histologic examination* revealed an ulcer with interruption in the muscularis propria and abundant sclerotic connective tissue. The pyloric musculature was hypertrophied, but the mucosa was intact and no notable sclerosis could be demonstrated.

Roentgen examination of the stomach should be given a broader aim than heretofore and directed towards a more detailed study of the gastric motivity. In such a study the stomach should not be overloaded with a heavy contrast medium, which causes distension, especially in the upright position, thereby precluding detailed visualization of the motive function. Manual compression during the fluoroscopic examination disturbs the gastric motivity. The hands need be used only to a slight extent. The examination should commence with the patient in the supine position and especially in the prone position, a rather small amount of contrast emulsion being employed. Valuable information concerning disturbances of motivity may be obtained through this procedure. A complementary investigation with the patient in the upright position, with greater contrast filling, is also necessary, however, to provide an all-round conception of the condition of the stomach. Particular care should be taken to visualize ulcers in the uppermost part of the longitudinal stomach, since these are easily overlooked. However, by observation of the gastric motivity it becomes easier to demonstrate ulceration. Local contractions in the inner muscular layer, with the characteristic triad of secondary changes arising therefrom, afford information concerning the part of the stomach in which the ulcer should be sought. In this way the examination becomes more methodical. If the typical local contraction remains after the healing of the ulcer, or if such a contraction is present without a demonstrable niche, it is justifiable to draw the conclusion that the gastric motivity is impaired. This implies a pathologic change in the function of the inner muscular layer of the stomach wall.

An ulcer in the longitudinal stomach appears to cause an increased contraction in the inner muscular layer. This muscular layer is distributed over the stomach like a contractile conductor cable. A 'spasm' arises corresponding to the extension of the inner muscular layer peripheral to the irritating agent, *i. e.* the ulcer. The anatomic extension of the inner muscular layer and its special structure, deviating from that of the other muscular layers, appears to make it useful as a conducting system for the gastric motivity. Inferior to its extension at the incisura angularis, another motive centre begins. Reasons for its occurrence have been brought out in modern physiologic study, and roentgenologically elucidated by the writer in an earlier work.

The inner muscular layer has previously been regarded as a part of the suspensory apparatus of the stomach and of importance only as a vertical support for the stomach, thus acquiring the name of a 'suspensory sling'. It is clear, however, that it is also of significance in the gastric motivity, a function of more importance. This function agrees rather well with the function of the special functional tissue of the heart. The writer therefore suggests that the inner muscular layer be called the inciting muscle as a part of the conducting system of the stomach. This conduction system should then also include the motive centre in the incisura angularis. Possibly there are still other, as yet unestablished components, in this conducting system. Although from the physiologic point of view it would be desirable to assume the existence of a motive centre also in the cardia, no roentgenologic proof has as yet been obtained.

In the heart the motivity originates and is transmitted through the special functional tissue which regulates the work of the heart musculature. In the stomach as well, it must be kept in mind that all muscular layers contribute to the motive effect, which is regulated by the conducting system. In ulceration of the longitudinal stomach, the lesser curvature is usually markedly contracted. The term 'schneckenförmige Einrollung' is used. The strong bundles of the inciting muscle are, of course, situated near the lesser curvature, but are however, also strengthened by a strong muscular band belonging to the outer longitudinal muscular layer: the medial longitudinal fasciculus. This is also affected, in all probability, by impulses from the conducting system, thus strengthening the contraction of the lesser curvature.

In gastric ulcers affecting the inciting muscle, spasms occur in a situation corresponding to the extension of this muscle. One question that cannot yet be answered is the cause of the occurrence of the spasm. It has only been possible to establish that it occurs in conjunction with gastric ulceration; and in the present discussion the ulcer has been regarded as being the cause. However, on the other hand, the possibility exists that a local spasm is significant in the pathogenesis of the ulcer. For example, it is conceivable that an abnormal contraction causes ischemia of the gastric wall, through which it becomes vulnerable to damage from the acid stomach contents. Subsequently, the ulcer gives rise in turn to further contraction. Such a vicious circle would explain both a poor tendency to healing in an ulcer and an inclination to recurrence.

It is well known that ulcers in the longitudinal stomach are usually situated on or near the lesser curvature. It is in this region, of course, that the local spasm is most pronounced. It is therefore quite possible that there is a connection between the predilection of the ulcer for the

lesser curvature and the muscular spasm or the conditions associated with such.

No plausible explanation of the origin of the pain associated with ulceration has been possible up to now, inasmuch as the gastric mucosa is not directly sensible to pain. Ulcers of appreciable size are sometimes observed roentgenologically, which give only slight pain; while, on the other hand, even small ulcers at times cause considerable distress. It is well known, however, that abnormal contractions of smooth muscles may give rise to severe pain. This fact is recognized in spastic colitis, in prestenotic intestinal contractions, in uterine pain and in the passage of stones. The occurrence of local spasm in the gastric wall appears to afford a possibility, in any case, of explaining the origin of the pain of ulceration.

SUMMARY

The inner oblique muscular layer has formerly been regarded as serving as a vertical supporting apparatus for the stomach. It appears to have a much greater significance, however, as the regulator of gastric motivity, and therefore is called the inciting muscle.

In ulceration of the longitudinal stomach, which affects this inciting muscle, contractions occur in that part which lies below the site of ulceration. These spasms give rise to characteristic changes demonstrable on roentgen examination. So-called 'gastritis' also appears principally to arise through such spastic contractions.

The inciting muscle in the longitudinal stomach, as well as the motive centre in the incisura angularis observed earlier by the writer, appear together to comprise, or at least to be the essential parts of, a conducting system which regulates the motivity

ZUSAMMENFASSUNG

Früher war man der Ansicht, dass die innere schräge Muskelschicht dem Magen als vertikaler Stützapparat dient. Sie scheint jedoch eine viel grössere Bedeutung als Regulator der Magenmotilität zu haben und wird daher Anregungsmuskel genannt.

Beim Ulkus des Längsmagens, das diesen Anregungsmuskel angreift, treten Kontraktionen in dem unterhalb des Geschwüres liegenden Magenabschnitt auf. Diese Spasmen geben Anlass zu charakteristischen Veränderungen, die röntgenologisch darstellbar sind. Auch s. g. »Gastritis« scheint hauptsächlich durch derartige spastiche Kontraktionen zu entstehen.

Der Anregungsmuskel im Längsmagen sowie das vom Verf. schon früher beschriebene Bewegungszentrum in der Incisura angularis scheinen zusammen ein Hauptsystem zu bilden, welches — zu mindesten in wesentlichen Teilen — die Motilität reguliert.

RÉSUMÉ

On a admis jusqu'à maintenant que la couche musculaire oblique interne sert d'appareil de soutien vertical à l'estomac. Elle semble cependant avoir une importance beaucoup plus grande comme régulateur de la motricité gastrique; en conséquence, l'auteur l'appelle «muscle incitateur».

Dans les cas d'ulcère de la portion verticale de l'estomac qui affectent ce muscle incitateur, des contractions locales se produisent dans les parties situées au-dessous de l'ulcère. Ces spasmes localisés donnent lieu à des modifications caractéristiques visibles à l'examen radiologique. Ce qu'on appelle «gastrite» semble être causé principalement par des contractions de ce type.

Le muscle incitateur de la portion verticale ainsi que le centre moteur de l'incisure angulaire décrit précédemment par l'auteur semblent constituer à eux deux, ou, au moins, être les éléments essentiels, d'un système d'incitation réglant la motricité de l'estomac.

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THE DIAGNOSTIC VALUE OF HYSTEROSALPINGOGRAPHY IN TUBAL PREGNANCY

by

Kristina Ekengren and *Åke B. V. Rydén*

In many cases of tubal pregnancy, the course is protracted and without characteristic symptoms. The objective signs are difficult to interpret correctly. Hysterosalpingography often facilitates diagnosis in these patients. Furthermore, there are cases where a hysterosalpingographic examination yields the typical picture of a tubal pregnancy even where there has been no reason to suspect this condition on clinical examination.

Cases in the Literature diagnosed with Iodized Oil

Hysterosalpingography as a method of examination in cases of tubal pregnancy was described for the first time by DYROFF (1926). The author considered unilateral tubal occlusion in association with uterine atony without signs of an intra-uterine ovum defect to be typical of tubal pregnancy. SCHNEIDER and EISLER (1927) based their opinions on ten cases of tubal pregnancy studied by radiography. They gave the chief diagnostic signs as (1) "eine intermittierende, segmentale Füllung"; (2) "eine sich trompetenförmig verbreitende Füllung"; and (3) "neben dem Schattenbild der verschlossenen Tube einzelne unregelmässig gelagerte Schattenflecke." Iodized oil was used as the contrast medium. POPOVIĆ and SMOKVINA (1928) also used iodized oil as their contrast medium in salpingographic examinations. The radiographic appearances stated by them as being characteristic of tubal pregnancy are similar to those mentioned by SCHNEIDER and EISLER. Only five of their twenty-three cases

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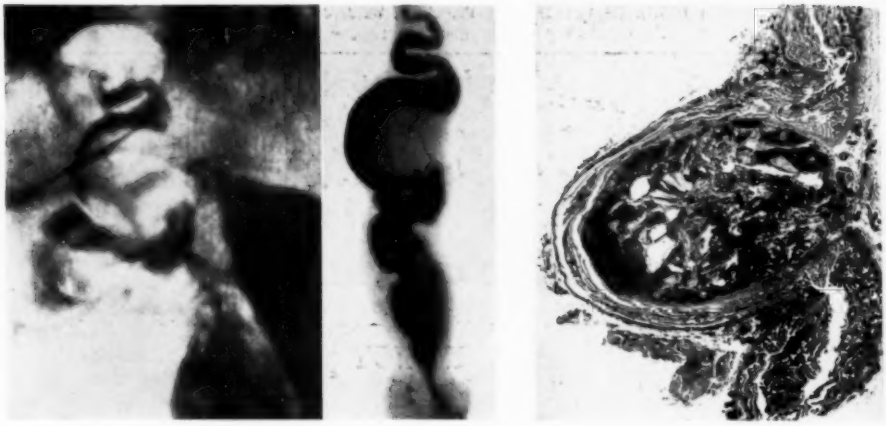
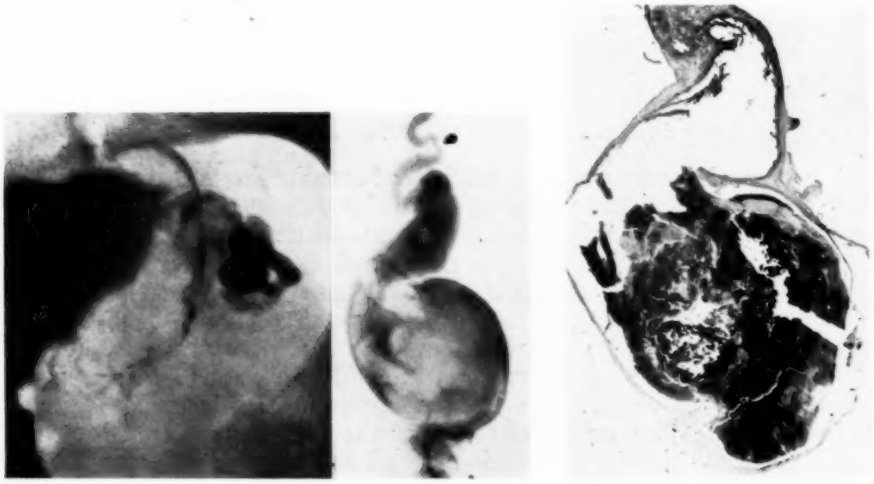


a. b. c.

Fig. 1. The ovum is surrounded by the contrast medium (a). It is implanted in the proximal portion of the ampulla (b). It is infiltrated with blood at the periphery but is fairly intact in the centre (c). The contrast medium has flowed along the cleft formed at the site where the ovum has broken away from the tubal wall.



a. b. c.

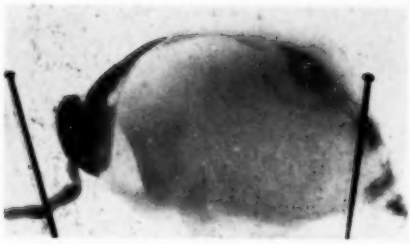
Fig. 2. The blood mole is situated in the distal part of the ampulla (a, b). The contrast medium has not only flowed along the cleft between the blood mole and the tubal wall but has also partially penetrated into the blood mole (c).

Fig. 3. The blood mole is situated in the distal part of the ampulla and is partially surrounded by the contrast medium.

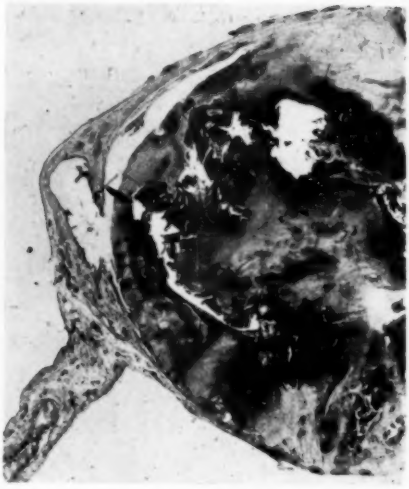
were verified by operation, however. VIALLET and JAHIER (1927) and RUCKER and WHITEHEAD (1928) report one case each in which tubal pregnancy was diagnosed from roentgenograms. SCHULTZE (1939) has described twenty-five cases of tubal pregnancy. In thirteen of these, the contrast medium (iodized oil) flowed out into the pregnant tube. The author stressed the fact that, in his opinion, the risk of making an incorrect diagnosis is great.

Cases in the Literature Diagnosed with a Water-Soluble Contrast Medium

GALEWSKI (1942) and MARSHAK (1946) described the roentgen appearances in two cases (one case each) of tubal pregnancy verified at operation. Both of these authors used a water-soluble contrast medium. NIELSEN (1947) published a report on twelve cases of tubal pregnancy studied by hysterosalpingography with the aid of a water-soluble contrast medium. He divides the radiographic appearances in the tube into three groups. In these, the contrast medium to a greater or lesser degree

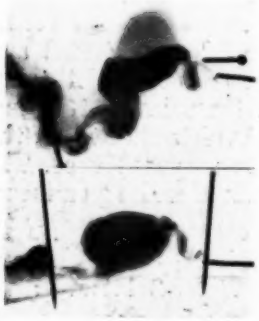


a.

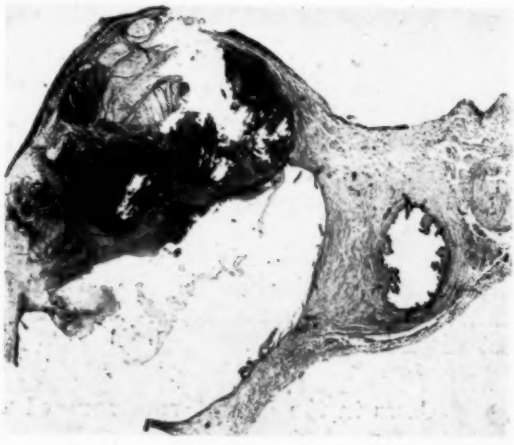


b.

Fig. 4. A surgical specimen filled with contrast medium (a) which is partially enveloping the blood-filled ovum.



a.



b.

Fig. 5. A contrast-filled surgical specimen from a tubal pregnancy situated in the tubal isthmus (a). The ovum, which is partially haemorrhagic, is implanted in the wall of the tube itself (b).

surrounds the blood mole in the lumen of the tube and produces pictures that are so characteristic as to allow a roentgen diagnosis to be made. SKJOLDBORG (1948) and LAWRENCE (1952) described three cases and one

case of tubal pregnancy, respectively, where the characteristic defect in the water-soluble contrast medium, due to the blood mole, made a correct diagnosis possible. In common with DE ALMEIDA (1951) these two investigators considered that hysterosalpingography is a valuable aid to diagnosis in cases of tubal pregnancy.

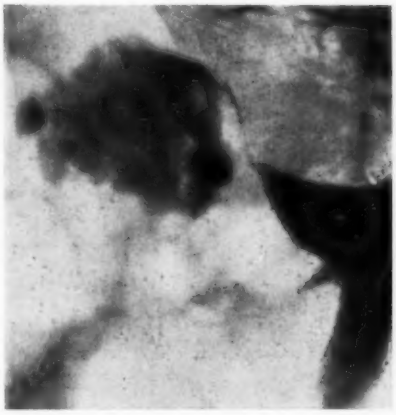
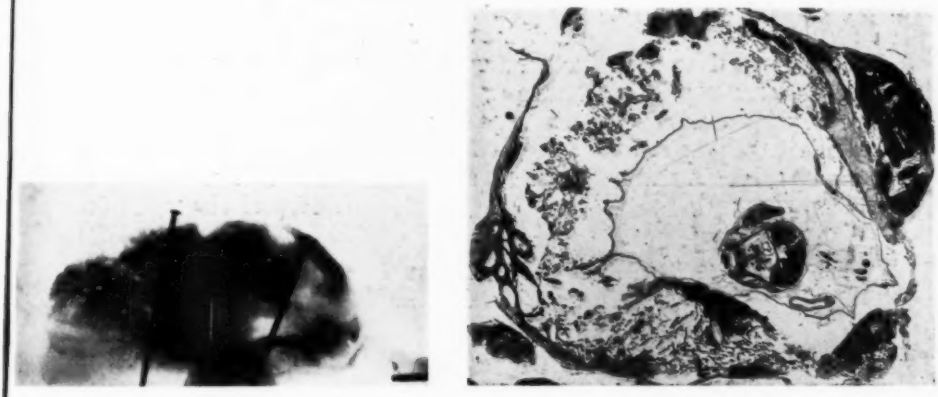


Fig. 6. The tubal pregnancy in the ampulla has been penetrated by the contrast medium (fig. 7 is the anatomic counterpart to the roentgen film).

Personal Material

Our investigation was based on twelve cases of tubal pregnancy examined by hysterosalpingography with the aid of a water-soluble contrast medium and verified both at a subsequent operation and by histologic examination. In some of these cases, the surgical specimen, after the injection of a contrast medium into the tubal lumen, was examined by radiography and then sectioned for histologic study. In a further eight cases in which no pre-operative hysterosalpingographic examination had



a. b.

Fig. 7. A contrast-filled surgical specimen from a tubal pregnancy in the ampulla (a), where the contrast medium has spread through the intervillous spaces (b). The photomicrograph shows an obliquely cut foetus at the centre. There are large defects in the contrast medium (a) due to small haemorrhages in the ovum (b).

Fig. 8. Tubal pregnancy in the ampulla (fig. 9 is the anatomic counterpart).

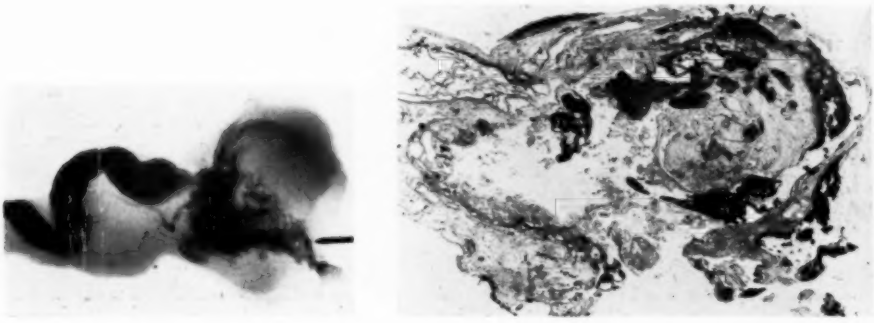
been carried out but in which a tubal pregnancy was established, the surgical specimen was examined in the manner indicated above.

We found that the roentgen appearances could be divided into two types:

1. The contrast medium to a varying degree enveloped the blood mole in the lumen of the oviduct without infiltration. The dye entered the lumen through the cleft that had formed where either the ovum, destroyed through partial haemorrhage, or the blood mole, had broken away from the distended wall of the oviduct (figs. 1, 2, 3, 4, 5).

2. The contrast medium spreads either diffusely through the intervillous spaces in the partly intact ovum (figs. 6, 7, 8, 9) or through larger channels in the blood mole (fig. 10).

Finally, there are radiograms that show transition stages between these two types (fig. 11).



a. b.

Fig. 9. A contrast-filled surgical specimen from the tubal pregnancy in the distal part of the ampulla (a). The contrast medium has not only penetrated into the intervillous spaces but has also to some extent enveloped the partially haemorrhagic ovum (b).

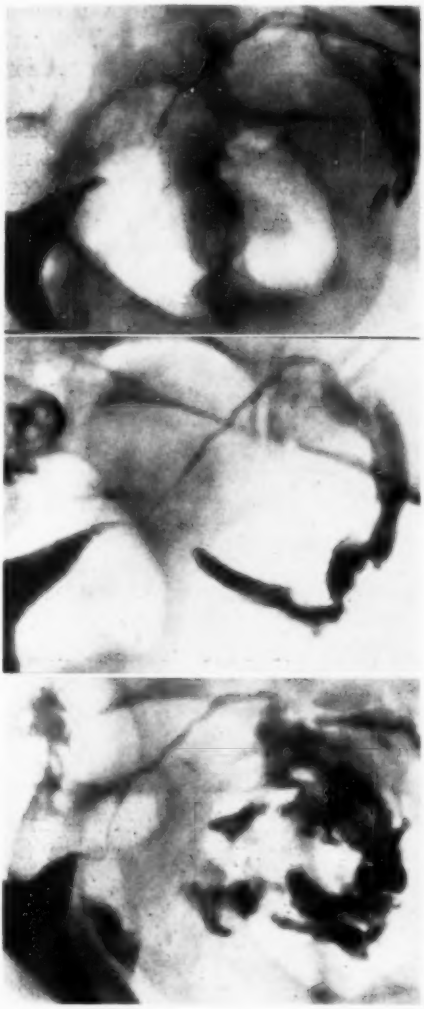


Fig. 10. A hysterosalpingogram of a tubal pregnancy in the ampulla, showing the contrast medium gradually spreading in the larger channels of the blood mole.

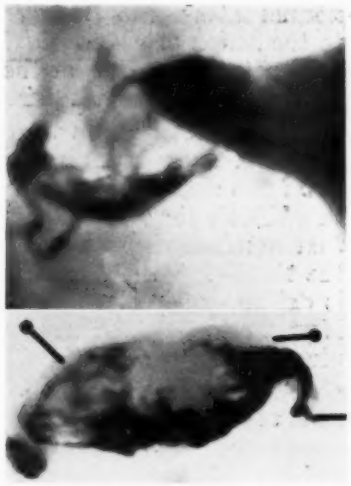


Fig. 11. The tubal pregnancy is situated in the ampulla (a). The ovum, almost entirely diffused with blood, is partially enveloped by the contrast medium which has also spread to the larger channels in the blood mole.

Discussion

The uterine atony described by earlier investigators (DYROFF, SCHNEIDER and EISLER, RUCKER, and others) as being a characteristic feature, and clearly visualized in hysterograms in connection with intra-uterine pregnancy by several authors, was not observed in our investigation. In ten of our twelve cases there were no signs of uterine atony while in two cases slight uterine hypotonicity was apparent in the hysterogram. Similar findings have been reported by SCHULTZE, NIELSEN, and others. The contracted isthmus reported by ASPLUND (1952) as occurring consistently in connection with

normal intra-uterine pregnancy and demonstrated by him as being due to the action of progesterone was not present in any of our cases. This is only natural, in view of the fact that intermittent uterine contractions nearly always take place in a tubal pregnancy.

These investigations are in keeping with the observations described by NIELSEN. Those investigators who used iodized oil as their contrast medium also obtained roentgenograms very similar to ours, but they report, in addition, findings which can hardly be interpreted as anything other than artefacts that had arisen owing to the oil having mixed poorly with the tubal contents. Our opinion, that the water-soluble contrast medium is definitely superior to iodized oil accords with NIELSEN's view. Like NIELSEN too, we did not have any complications after the hysterosalpingographic examinations.

For a roentgen diagnosis to be possible it is necessary that the pregnant tube should be patent to the contrast medium. NIELSEN describes a case where this did not apply. In our material, there were two cases in which the tube was so poorly filled with dye that it was not possible to make a diagnosis (these two cases have not been included in this report).

The investigation showed that, in the majority of cases of tubal pregnancy, a roentgen diagnosis is possible with the aid of hysterosalpingography, and this method is therefore useful in doubtful cases.

BORELL, FERNSTRÖM and WESTMAN (1953) have described a radiologic investigation based on retrograde arteriography by way of the femoral artery. This method can also be used to diagnose tubal pregnancy by filling the blood vessels and intervillous sinuses with contrast medium. In one of our previously described cases where a diagnosis was not possible with hysterosalpingography, this method gave a positive result. These two methods are complementary in the diagnosis of cases of suspected tubal pregnancy. A knowledge of the salpingographic features in this form of pregnancy is necessary in view of the fact that, as has already been mentioned, tubal pregnancy may be encountered after a hysterosalpingographic examination without this diagnosis having previously been suspected.

SUMMARY

In twelve cases of tubal pregnancy verified at operation the authors show that hysterosalpingography gives such typical appearances in the majority of cases that a diagnosis can be made from the roentgenograms. Variations in the salpingographic features are illustrated by roentgen films and sections from the surgical specimens.

ZUSAMMENFASSUNG

In 12 Fällen mit operativ verifiierter Tubenschwangerschaft zeigen die Verf., dass die Hysterosalpingographie in der Mehrzahl der Fälle ein derart typisches Aussehen zeigt, dass die Diagnose auf Grund der Röntgenbilder gestellt werden kann. Variationen des charakteristischen salpingographischen Befundes werden durch Röntgenaufnahmen und durch Schnitte der chirurgischen Präparate illustriert.

RÉSUMÉ

Les auteurs montrent que, sur douze cas de grossesse tubaire vérifiés opératoirement, l'hystérosalpingographie a donné dans la majorité des cas des aspects si typiques que le diagnostic peut être fait sur les radiographies. Des radiographies et des coupes des pièces opératoires illustrent les variations des signes salpingographiques.

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ROENTGEN INVESTIGATIONS OF THE NEO-NATAL GASEOUS CONTENT OF THE INTESTINAL TRACT

by

Johan Frimann-Dahl, John Lind and *Carl Wegelius*

The roentgenologic demonstration of gas in the stomach and the intestines of the new-born may be used for several diagnostic purposes. In forensic medicine, gas in the intestine is used as a sign of neo-natal life. The great importance of intestinal gas as a diagnostic criterion in acute abdominal lesions, occlusions, obstructions, congenital malformations etc. is well known.

The whole question of origin of gas in the intestinal tract can be elucidated by studies of its initial appearance. During intrauterine life, the fetus swallows amniotic fluid which is sucked into the stomach and small intestine. It may pass over into the colon taking part in the formation of the meconium. It is also resorbed from the gut and excreted through the kidneys. This has been proven by roentgen studies after the intrauterine injection of thorium, in guinea pigs by BECKER, WINDLE, BARTH and SCHULTZ, in monkeys by SPEERT and in human fetuses by DAVIES and POTTER. The contrast medium may be observed passing through the esophagus into the stomach and the bowel, and small quantities of the medium may also pass over into the lungs. From such examinations the conclusion may be drawn that the ability to swallow is probably developed before the ability to breathe.

The observation has also been made that the time of passage through the gut is decreased as the fetus increases in size. In health, as soon as the child is born it starts breathing and air is pulled into the lungs. Simultaneously, and even before breathing has started, air is also drawn into the esophagus and stomach by sucking movements of the mouth

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and is propelled further down into the bowel. This procedure has certainly been known for a long time and has been taken into account in forensic medicine to estimate the duration of life of the new-born. In autopsy specimens, various parts of the gut have been examined to determine the gaseous content of the viscera. By means of a simple test as to whether or not the stomach or parts of the gut float in water, the amount of gas may be roughly estimated. This is known as BRESLAU's *test* and has been used in forensic medicine since 1866. BRESLAU postulated that the investigation could show exactly whether the child had been alive or not, and also help to determine the amount of respiratory activity. This last premise, however, has been opposed by many authors and has been much disputed in the literature.

Experience has taught us that respiration and air-filling of the lungs may be restrained or completely inhibited by mucous aspiration into the bronchi. In such cases (when the lungs are atelectatic), swallowed air, when disclosed in the stomach and small intestine, may give decisive proof of life.

HARBITZ (1906) has dealt with this from the pathologic and forensic points of view based on post-mortem examinations in a number of cases shortly after birth (roentgen examinations were employed). Autopsies on children who had been alive 15 minutes after birth usually showed gas in the stomach. After from two to six hours this had penetrated into the small intestine and even to the large bowel. This latter was the general rule if the child had been alive for 12—24 hours. HARBITZ came to the conclusion that an exact determination of the gaseous content of the stomach and intestines compared with the amount of air in the lungs was a most valuable sign in the estimation of the duration of life.

Although the significance of demonstrating gas in the intestinal tract in new-born had been stressed by many authors, the radiologic literature made no reference to it until 1942 when DILLON stated that the roentgen examination was the most practical means of demonstrating gas in the stomach and intestines; accumulation of gas in the stomach was proof of life, and might be present even if no air was detectable in the lungs. He also showed that gas in the stomach and small intestines was visible not only in full-term infants, but might be seen in fetuses down to 20 weeks of age. However, he claimed that the gas was air which had not been swallowed, but that a kind of intestinal respiration took place, pulling it down into the stomach and intestines. DILLON's explanation of the origin of the intestinal gas has not been entirely supported. On the contrary ANDERSEN and RINGSTED demonstrated by means of a series of cases of experimental ileus that the accumulation of gas in the small intestine was due exclusively to swallowed atmospheric air. Among others, supporting this conclusion were MAGNUSSON and ENGSTRÖM, who investigated

aerophagia in infants with special reference to the disturbing effect of meteorism in urography.

WASCH and MARCK (1948), also assumed that air is present in the stomach immediately after birth. They claimed that a survey of the available literature failed to disclose any investigations describing the progression of this air. For this purpose, radiologic examinations, beginning from 1/2—1 hour after birth, were carried out during the first day of life. The findings concerning the distribution and passage of air in the different parts of the gastro-intestinal tract were collected in a table showing how it advanced from 1/2—24 hours after birth. No conclusions were drawn regarding the origin and first appearance of intestinal gas. This may have been due to the absence of examinations during the first 1/2 hour after birth. Neither HENDERSON (1942) nor MIDDLEMISS (1950) discuss the origin and very early progression of intestinal gas in their communications on the radiologic detection of occlusions and malformations in the new-born. The monograph by SOVERI (1939) on the physiologic progression of intestinal gas in infants does not deal with the first of life.

Finally it should be mentioned that gas may develop in the circulatory system in fetal death. This has been demonstrated by many authors and KETTUNEN suggests the RH factor in the blood as the source of decomposition. However, air in the vessels and air in the intestinal tract should be easily distinguished on the films and mistake is unlikely.

Even though such examinations have been undertaken previously, we hold the opinion that more systematic observations on a larger material are necessary. It may thus be necessary from forensic and physiologic as well as clinical aspects, to investigate what happens to the intestinal gas at the moment of birth and immediately afterwards. The more important questions are:

1. Is there intestinal gas present at birth?

2. If not, when does the first gas appear and what is its relationship to the first appearance of air in the lungs?

3. Can any conclusions, based on the previous question be drawn regarding air swallowing as the cause of intestinal gas?

4. How rapid is the passage and the distribution of intestinal gas during the first minutes and hours after birth; has this any significance in the estimation of the duration of life?

In order to answer these questions, serial radiography as soon as the birth has taken place is indicated. Two films should be obtained synchronously at right angles in order to permit of a three-dimensional evaluation of the morphology and topography of the esophagus, stomach and the

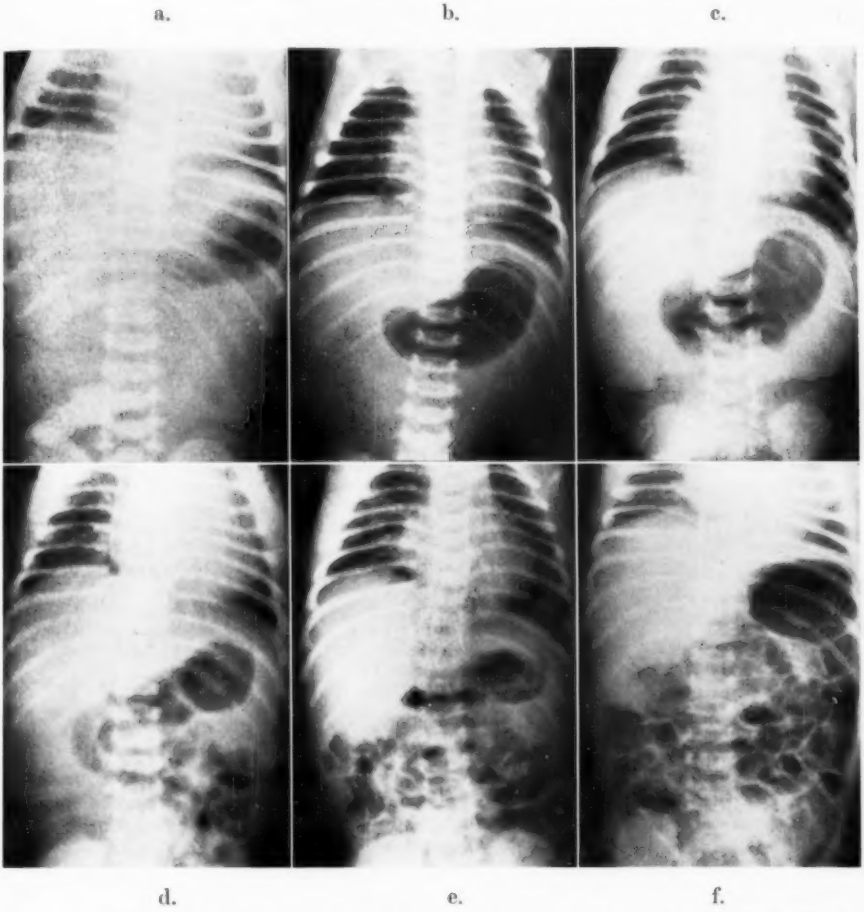


Fig. 1. Typical distribution of air in the intestinal tract immediately after delivery and the nearest hours. (A-p views). — a. Lungs slightly air-filled. Gas has descended into the stomach. — b. After 15 min: Stomach expanded by gas. — c. After 30 min: Gas has penetrated the pylorus and entered the duodenum and prox. jejunum. — d. After 1 hour: Jejunum gas-filled. — e. After 2 hours: Stomach and entire small intestine filled with gas. — f. After 7 hours: Fully developed 'physiologic meteorism'.

other gas-filled parts of the digestive tract. On the one hand, it is important to take films at sufficiently short intervals in order to catch the dynamic progression of the gaseous filling and, on the other hand, to avoid any harmful irradiation effect on the sensitive human subjects.

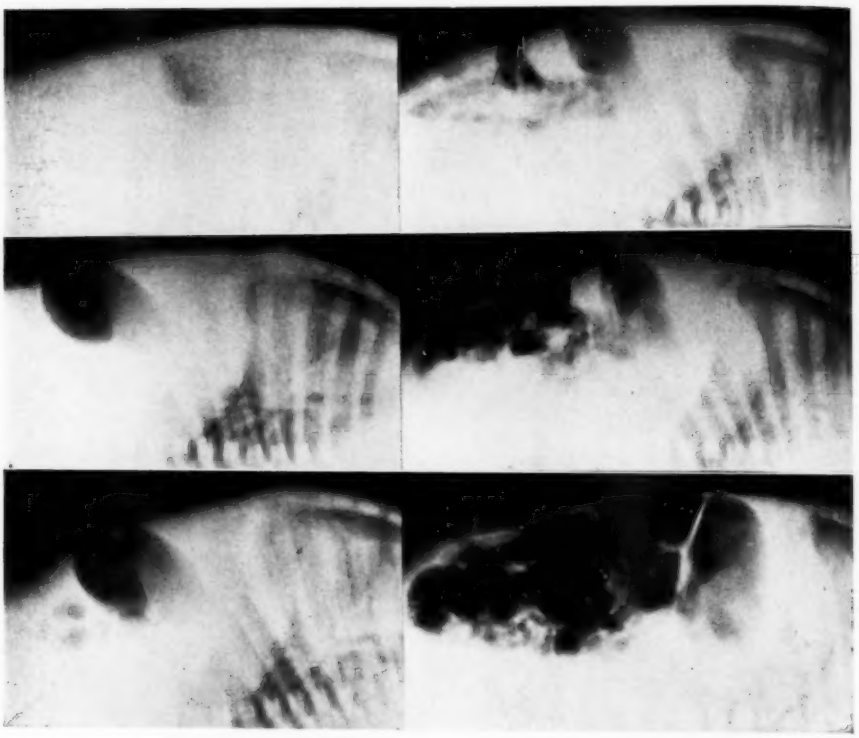


Fig. 2. New-born infant (Lateral views). — a. Shortly after birth: Small air-bubble in the stomach barely visible. Lungs sparingly air-filled. — b. After 15 min: Stomach expanded by air. Lungs better filled. — c. After 20 min: Air has penetrated into the duodenum. — d. After 1 hour: Stomach, duodenum and jejunum air-filled. — e. After 2 hours: Whole of small intestine air-filled. — f. After 7 hours: 'Physiologic meteorism'.

Own Investigations

Our investigations are based on a material of 20 new-born infants examined at the South Maternity Hospital in Stockholm with the above points in mind. A roentgen apparatus with two tubes and with facilities for synchronous exposures at right angles was installed close to the delivery room. The infants were transferred to the roentgen couch as soon as the umbilical cord had been cut. This necessary procedure delayed the first roentgenogram for about one minute after the true instant of birth. Consequently, all the infants had cried and the lungs were already filled with air at the first exposure; without exception serial films were also

obtained at 15, 30, 45 minutes and 1, 2 and 3 hours following birth. The complete series, consisting of two exposures upon each occasion produced an individual irradiation dosage in toto of between 1.4 r units, a value which may be considered as lying far below the limits of tolerance.

All the babies were delivered at term and were healthy and well-formed. The findings were in some way stereotyped. Soon after birth a small air-bubble was seen lying in the stomach, filling the fundus and the corpus, but no air was visible in the duodenal bulb (Figs. 1—2). The size of this air-bubble varied a great deal. In one case it was barely visible and in others the stomach was considerably expanded by the gas. In general, the distal parts of the intestinal tract was completely devoid of air or any gaseous content. In one case only, the gas had filled the stomach and the duodenum as well as the proximal part of the jejunum. Occasionally a narrow column of air passing down to the stomach could be recognised in the esophagus, a finding which is emphasized because in our opinion it confirms the theory that air is swallowed down by active sucking movements of the child.

After 15 minutes, the gas-bubble in the stomach usually increases in size, filling the viscus which is easily recognised by its shape and size. (Fig. 1 b). No gas has as yet penetrated through the pylorus.

After 30 minutes, air is visible in the duodenum and jejunum and may have reached the proximal portion of the ileum (Fig. 1 c).

After 1 hour, the air-bubble in the stomach may have decreased a little, but on the other hand the gas has been propelled further and has reached the terminal ileum (Fig. 1 d). It is very rare for the gas at this time to have reached the cecum.

After 2 hours, the air has traversed the small intestine and may have reached the cecum. A complete filling of the small intestinal loops gives the well-known pattern of polygonal translucencies surrounded by fine opacities corresponding to the intestinal wall.

After 3 hours, a 'physiologic meteorism' has usually developed and the gas fills the entire intestinal tract. Between 2—3 hours, variations

Table 1

Showing average distribution of intestinal gas after delivery in full-term healthy children

	Partus	15 min.	30 min.	45 min.	1 hr.	2 hrs.	3 hrs.
Lungs	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+
Duodenum	÷	+	+	+	+	+	+
Jejunum	÷	+	+	+	+	+	+
Ileum	÷	÷	÷	+÷	+÷	+	+
Cecum	÷	÷	÷	÷	÷	+÷	+
Colon	÷	÷	÷	÷	÷	+÷	+

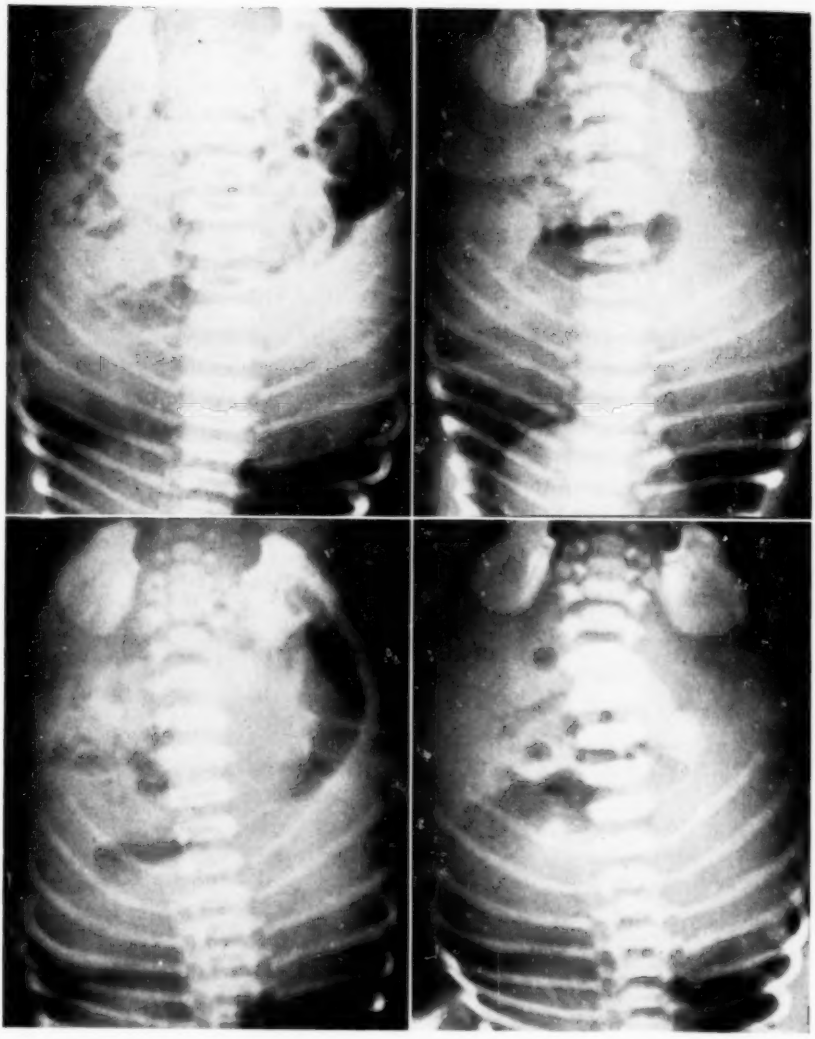


Fig. 3. No influence of crying. Films a_1 a_2 show a silent infant 15 min. and 3 hours after birth, resp., b_1 b_2 are of an infant crying continuously at the same intervals. The gaseous content is seen to have reached the same intestinal regions at the corresponding times.

in the gaseous content of the colon may be observed and the discharge of flatus occurs.

Typical findings concerning appearance, distribution and passage of intestinal gas are noted in Table 1. This shows that soon after birth, gas is usually present only in the lungs and stomach. From the stomach, the air penetrates the pylorus and passes into the small intestine and, after 3 hours, the physiologic meteorism of the new-born healthy child is generally complete.

Regarding the progression of intestinal gas in the new-born, there is one factor which has not previously been discussed — the possible influence of crying. We therefore compared a control series of examinations of silent infants with others crying vigorously. We could find no difference to confirm the theoretically possible effect of crying on progression (Fig. 3).

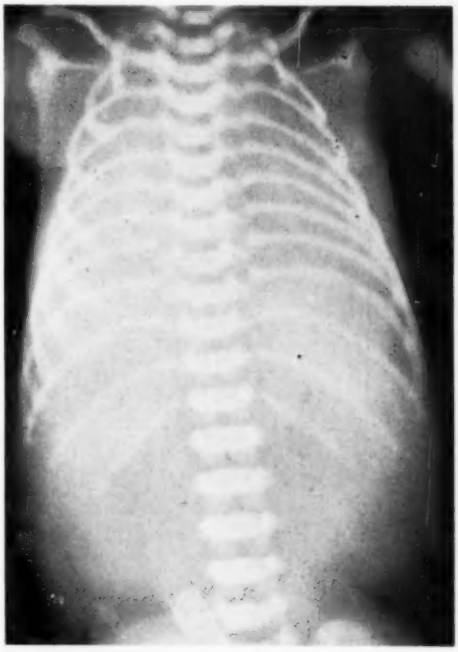
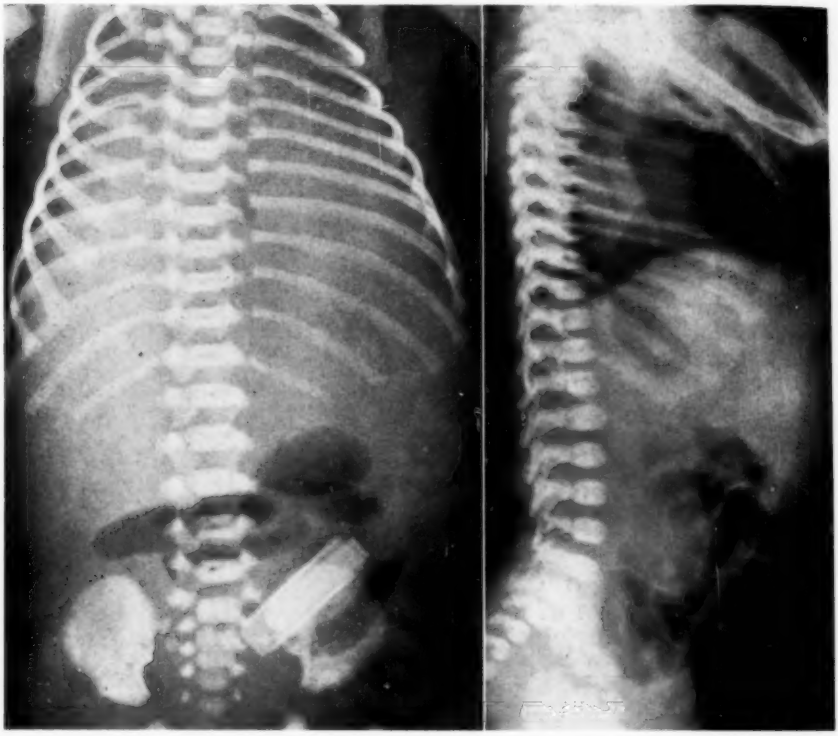


Fig. 4. Still-born infant. Atelectatic lungs, no air in the intestinal tract.

Post-mortem Findings

In addition to our investigations of living babies, 15 newborn infants (forensic cases) from the Pathologic Institute, Ullevål Hospital, Oslo (Chief Prosector: E. Hval) were examined and the roentgen findings compared with those obtained by the Breslau test. The findings in general corresponded well to the appearances found in the examinations of living subjects and the conclusions drawn concerning the time of life proved to be quite correct. In one case (Fig. 5 a—b), for instance, it was decided that the child must have been alive for at least 2 hours. The lungs had filled and air had penetrated down into the stomach and small intestine and had reached the ileum. The Breslau test was positive, the upper portion of the small intestine and stomach floated in water and gas escaped when these organs were incised.

In feeble or under-developed infants, the findings do not appear to be

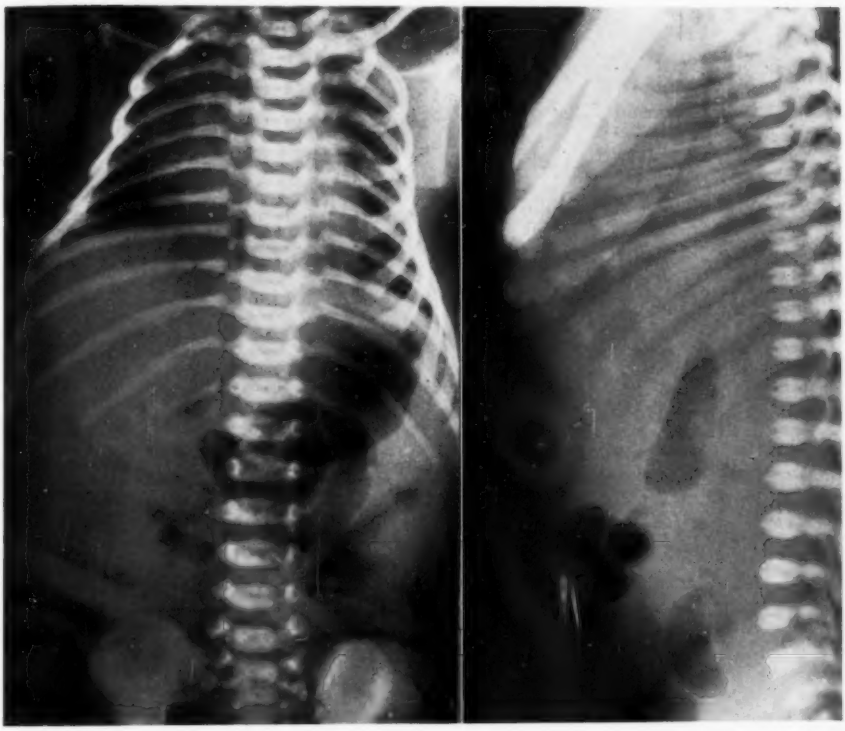


a. b.

Fig. 5. a—b. Forensic case. The child had been alive for about 3 hours. The roentgen findings suggested that the time of life must have been at least 2 hours. A-p and lateral views.

so reliable. In one case, there was doubtlessly some air in the stomach and in the small intestine as far as the ileum which would correspond approximately to the same living time, 2—3 hours (Fig. 6 a—b). The lungs were, however, atelectatic so that but very little breathing could have taken place. The only sign of this shown in the roentgen films was in the lateral view in which a little air in the trachea and smaller bronchi was just visible. The history revealed, however, that the child had been alive for ten hours.

In another case (Fig. 7), the lungs were atelectatic but air was visible in the stomach and small intestine as well as in the colon. This newborn had been alive for 48 hours; it was $7^1/_2$ months of age and definitely under-



a. b.

Fig. 6. Feeble infant alive for 10 hours. — a. a.p. view. Lungs atelectatic. Air in the stomach and jejunum. No gas in the colon. — b. Lateral view; some air is visible in the trachea and smaller bronchi.

developed. It can therefore be stated (1) that air may be found in the intestinal tract even if the lungs are atelectatic and (2) that atelectatic lungs probably mean that the child was feeble and only breathed superficially, the air in the intestine being propelled more slowly in these children than in normal and healthy babies. Hence, the duration of life should be especially carefully estimated when the lungs are collapsed and the child is under-developed. A similar statement was made by HARBITZ nearly 50 years ago. In this connection, it is also interesting to note the findings in a case of chondrodystrophic dwarfism (Fig. 8) in which the lungs were atelectatic and enclosed in a thoracic cage evidently unsuited for proper respiration. A little gas had collected, however, in the stomach and duodenum, and, microscopically, the lungs contained air. The child

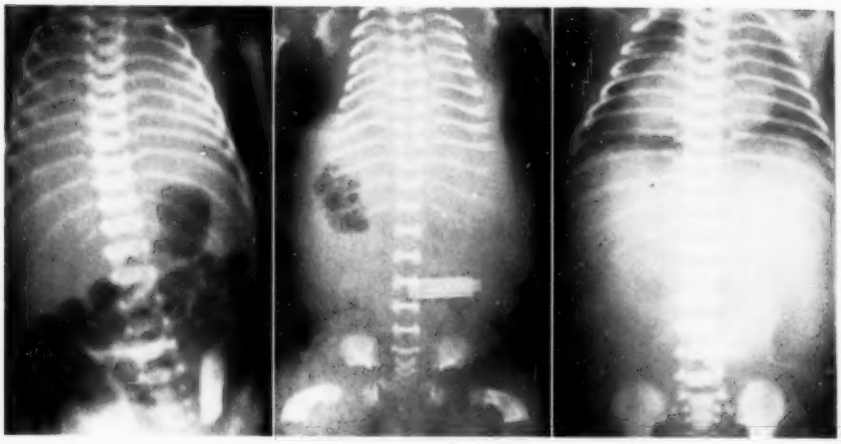


Fig. 7. Fig. 8. Fig. 9.

Fig. 7. Under-developed infant, alive for 48 hours. Lungs atelectatic, though parts floated in water (superficial breathing). Stomach and the entire bowel filled with gas.

Fig. 8. Chondrodystrophic dwarfism. Premature infant, alive for some minutes. Lungs atelectatic. Some air in the stomach.

Fig. 9. Spontaneous delivery. Cyanosed child, alive for some minutes. Lungs air-filled; no gas in the stomach.

had been alive for some minutes. Filling of the lungs with air but no gas in the stomach was observed in one case (Fig. 9). After spontaneous delivery, the cyanosed child was alive for a few minutes; it did not cry. At autopsy, the lungs proved to be aerated and floated in water; no air was detected in the stomach or in the bowel. Death was caused by cerebral hemorrhage. Artificial respiration was carried out for a time, but without result.

Finally, the question arises as to whether air can penetrate into the stomach following artificial respiration. We therefore also examined the effect of artificial breathing in still-borns. It proved to be impossible to detect any air in the stomach after swinging procedures or after active movements of the chest. The lungs remained as atelectatic and the stomach as empty as before.

Post-mortem roentgen examinations are easily performed. The subject is small and no breathing or movements interfere with the sharpness of the roentgenogram. The presence of gas is a very reliable sign of life and even the smallest amount is visible when satisfactory films are made in two different planes. The roentgen examination may be decisive

and, made as it should be before the opening of the cadaver, can be more reliable than the pathologic-anatomic examination. It will always give good support to an autopsy and should be undertaken in all forensic cases.

Conclusions

From investigations on living babies and post-mortem findings, the following conclusions seem possible:

1. No gas collects in the stomach or intestine during intra-uterine life. In still-born infants, no air visible either in the lungs or in the intestinal tract. If the infant is underdeveloped or feeble, it may have been alive for some time even though no gas is visible in the lungs or stomach. Immediately after birth, gas is usually present in the stomach whereas the remainder of the intestinal tract is completely devoid of gas.

2. Gas in the stomach appears immediately after birth, simultaneously with the expansion of the lungs. If the pulmonary breathing is inhibited and the lungs are atelectatic, the air may penetrate into the stomach, and is then a definite proof of life. The reverse situation, gas-filled lungs and no air in the stomach, appears to be rare; it was observed in one of our cases.

Gas in the stomach and intestinal tract immediately after birth originates from the swallowing of atmospheric air. It appears so quickly that putrefaction as a possible origin may be excluded.

4. The gas traverses the small intestine and reaches the colon at a fairly constant speed in the healthy new-born. Consequently an estimation of the duration of life by means of roentgen examination is quite reliable. The findings are in good agreement with investigations carried out on autopsy.

5. Even though the lungs from the roentgenograms appear completely atelectatic, air may be revealed microscopically or part of the lungs may float in water.

6. The roentgenologic demonstration of air in the stomach and intestines seems to be more accurate and reliable than in the case of the lungs.

SUMMARY

The occurrence of gas in the intestinal tract based on roentgen examinations in twenty new-born children and fifteen post-mortem cases is discussed. Swallowed air may be demonstrated immediately after delivery. The progress of the gas which takes place at a fairly constant speed is described; from it the duration of life may be roughly estimated. The importance of roentgen examinations in post-mortem and forensic cases is emphasized.

ZUSAMMENFASSUNG

Das Auftreten von Luft in den Dünndarmen wird diskutiert. Als Grundlage dienen Röntgenuntersuchungen von 21 neugeborenen Kindern und 15 Obduktionsfällen. Verschluckte Luft kann unmittelbar nach der Geburt dargestellt werden. Die Zunahme der Luftmenge, die mit einer ziemlich konstanten Geschwindigkeit geschieht, wird beschrieben; hierdurch kann die Lebensdauer grob geschätzt werden. Die Bedeutung der Röntgenuntersuchungen für Obduktionen und für gerichtsmedizinische Fälle wird hervorgehoben.

RÉSUMÉ

Les auteurs ont recherché radiologiquement la présence de gaz dans le tube digestif chez vingt nouveau-nés vivants et quinze morts. Il est possible de mettre en évidence de l'air dégluti aussitôt après l'accouchement. Les auteurs décrivent la progression des gaz qui a lieu à une vitesse assez constante et qui permet d'estimer grossièrement la durée de vie. Les auteurs soulignent l'intérêt des examens radiologiques dans les cas de mort et d'expertise médico-légale.

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EMPHYSEMATOUS CYSTITIS

by

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Emphysematous cystitis has been defined by R. G. MILLS (1930) as an inflammatory condition with gas-filled vesicles in the wall of the urinary bladder.

EISENLOHR (1888) was the first to observe this morbid condition as an incidental finding at autopsy. MILLS (1930) described twelve cases seen on autopsy, including the first instance observed in a man. Previous authors had held the view that the disease occurred only in women. Later observations have shown that MILLS's male case was not exceptional. The condition, however, is more common in women than in men, which is in keeping with the fact that cystitis in general is more frequent in women.

So far, the observations of this condition in living subjects has been reported only in a dozen cases. The first description was given as late as 1932, when RAVICH & KATZEN reported that at cystotomy on a man aged 56 with pronounced hematuria, they had observed the characteristic gas-filled vesicles in the mucous membrane of the bladder. ANTOINE (1934) was the first to diagnose the lesion by cystoscopy, and he was also able to confirm that the vesicles contained gas by pricking one and seeing the content bubble up towards the apex of the bladder.

Only two cases have been diagnosed primarily by roentgenography (LUND et al., 1939; TEASLEY, 1949); in the other cases in which the bladder was examined roentgenographically this was done only after cystoscopy. The writers are now able to add a third case to these two.

A woman (9/52 and 589/53), aged 55, had suffered from diabetes since 1951 and had been treated with diet and 20 I. U. of insulin daily. On examination in April 1952, infection of the urinary tract was discovered, and in June she had cystopyelitis on the right side; this subsided under treatment with sulfonamide. On admission to the Medical Clinic on the 29th August, 1952, on account of pain on the right side of the abdomen

and acute onset of fever, her general condition was not affected; abdomen soft and not tender to palpation. Temp. 38.2°; S. R. 76 mm/1 hr; urine: Heller's test negative; in the sediment an abundant number of white blood cells; Almen's test positive; growth of coliform rods, sensitive to streptomycin, chloromycetin and terramycin but resistant to penicillin and sulfathiazole. The patient was given streptomycin from the 10th to the 23rd September. Intravenous urography 12/9 showed that the right kidney was considerably smaller than the left, but neither kidney showed any functional abnormality; bladder apparently normal. Urography, repeated on the 18th September, now showed that the bladder represented a markedly swollen mucosa and the greatly thickened wall had a large number of roundish defects, varying in size from a pinhead to a pea, with a density corresponding to a gaseous content. The capacity of the bladder was markedly reduced (Fig. 2). The diagnosis of emphysematous cystitis was made (BOIJSEN).

The films of the bladder obtained on the 12th September were re-examined, and a sickle-shaped zone about 1 mm thick, corresponding in density to that of gas, was seen surrounding the diluted contrast medium in the upper and dorsal aspects of the bladder. The wall of the bladder seemed to be of average thickness, and the volume of the bladder normal (Fig. 1). Neither examination showed evidence of free gas within the bladder but films with horizontal beam direction were not taken.

One week later, cystoscopy showed the mucous membrane of the bladder to be inflamed and covered with several conglomerates of white glistening vesicles. This was confirmed by further cystoscopy one week later. Two weeks later, a roentgen examination of the bladder demonstrated gaseous vesicles only within a small area limited to the left wall of the bladder; the thickness of the wall now appeared to be normal, as was the capacity of the bladder. On the other hand, there now seemed to be a considerable amount of free gas in the bladder, in other words, a state of pneumaturia (Fig. 3).

Two weeks later, on the 20th October, urography was repeated and showed an additional increase in the capacity of the bladder, which now was abnormally large, with a smaller amount of gas in the lumen than at the preceding examination.

During retrograde pyelography on the 14th November, which revealed an insignificant anomaly of the right renal pelvis, further films were obtained of the bladder. This was again of normal dimensions and without any evidence of intramural gas; no signs of pneumaturia. The cystoscopy showed a reddish inflamed vesical mucosa, free from gaseous vesicles.

When the diagnosis had been made, urine cultures were obtained on several occasions. The bacteriologic examination again showed the presence of coliform rods that fermented glucose with the formation of gas, and grew anaerobically. At the same time, the presence of Proteus vulgaris and enterococci was demonstrated. The alcohol concentration in the urine was 0.15 % — a value that does not exceed the physiologic content.

The infection was treated with terramycin, chloromycetin and sulfathiazole, but cultures from the urine continued to show growth of coliform rods and Proteus vulgaris.

While there had been no previous evidence of hematuria or pneumaturia, on the 19th September, the day after the diagnosis of emphysematous cystitis had been made roentgenographically — macroscopic hematuria occurred and persisted in varying degrees until the 2nd October. On the 29th September the patient observed that a little gas was passed at the end of urination; and on catheterization on the 30th September a considerable amount of gas was drawn off with the specimen.

On the 22nd November, the patient was discharged free from urinary symptoms and without microscopic pyuria. She was readmitted on the 4th March, 1953 with fever and with pain in the right side of the abdomen. Since her discharge she had noticed no blood or gas to the urine.

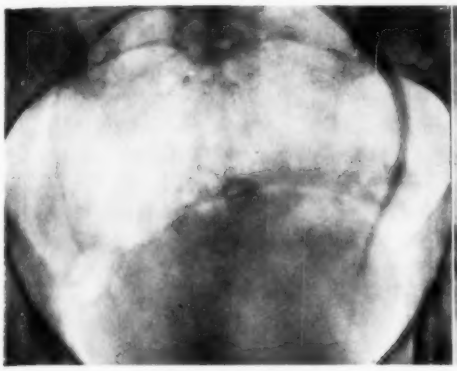

Fig. 1. 12th September. Bladder of normal size, surrounded by a 1 mm sickle-shaped zone of gas. It differs from the fat layer often seen in that the radiolucent zone is irregular and reaches far down on both sides.

Fig. 2. 18th September. Capacity of the bladder greatly diminished. The markedly thickened wall of the bladder is studded with small gaseous vesicles.

Fig. 3. 7th October. Pneumaturia present. Bladder of average size with a wall of normal thickness. A mere suggestion of gaseous vesicles can still be made out in the wall, to the left.

Fig. 4. 20th October. The vesical mucosa contains no gas. The horizontal projection reveals pneumaturia with a layer of gas about 1 cm in depth. The bladder is markedly distended.

On readmission the temperature was 38.3° and the urinary sediment contained a considerable number of white blood cells. This time the bacteriologic examination of the urine showed the presence of only Proteus vulgaris, no coliform rods being found.

The patient was given chloromycetin and sulfametin and on the third day her temperature was normal; on the same day she passed two concretions. Discharged, 14th March, feeling perfectly well.

Discussion

All authors agree that infection is the *cause* of emphysematous cystitis. A well-known producer of gas in the tissues — the Welch-Fränkel gas gangrene bacillus — could be demonstrated on autopsy in a majority of the cases as the cause of emphysematous cystitis (Göbel, 1893; Welch & Flexner, 1896; Weiser, 1929). In more recent years, however, cases have been described in which the gas gangrene bacillus could with certainty be considered the cause of the infection, and yet the patient recovered (Antoine, 1934; Levin, 1938). Some authors, it is true, believe that a distinction should be made between emphysematous cystitis and gas gangrene of the bladder wall and that the latter affection should be attributed to the Welch-Fränkel bacillus. But, as the clinical picture is the same in both conditions which can be differentiated only by means of bacterial cultures, such a classification does not seem justified at present.

The most common cause of emphysematous cystitis, however, is to be found in the presence of coliform bacteria which in most cases have been demonstrated by cultures from the urine of patients under clinical observation. Unfortunately, the bacteria found in this way have not always been examined as to their capacity for gas production; several observations indicate that the presence of glucose is necessary. Normally, 20—40 mg % glucose occurs in the wall of the bladder; in diabetics, this percentage may be considerably higher. Furthermore, it is also in diabetics that emphysematous cystitis is observed most frequently. Some cases are even reported in which the patients were given considerable amounts of glucose just before death (Mills, 1930; Sanes et al., 1934; Wells, 1938). Lund et al. (1939) were able, by puncture of the bladder, to collect and analyze the gaseous content and demonstrate that it consisted of carbon dioxide. Schönberg (1913) was able experimentally to show that colibacteria from a patient with emphysematous cystitis produced similar changes in animals without any increase in the sugar content of the tissues. He was also able to show that the capacity of the colibacteria for gas production decreased as time went on. Taussig (1907) raised the question whether the gas-producing capacity of B. coli might not be associated with a development phase of the bacteria. Thus the occurrence of gaseous vesicles in the inflamed vesical mucosa becomes limited to a certain stage of the cystitis. The case observed by us lends support to the correctness of this view. Additional evidence to

this effect is found in the frequency of emphysematous cystitis in proportion to the incidence of colibacterial cystitis in general.

The development of emphysematous cystitis, however, does not depend exclusively on the inflammation-producing characters of the bacteria but — as in all infections — also on local and general conditions. Hitherto, emphysematous cystitis has been observed most often in patients with impairment of their general condition. Our present knowledge of the etiology and pathogenesis of emphysematous cystitis may be summarized by saying that it is brought about primarily by bacteria belonging to the colon group, that diabetes mellitus promotes its occurrence and that it appears to be a condition of cystitis rather than a disease sui generis.

The *pathologic-anatomic* changes have previously been described particularly by MILLS (1930) in the Anglo-American literature and by JÖNSSON (1946) in the Scandinavian. On inspection, the entire vesical mucosa is studded with glistening vesicles varying in size from pinheads to peas. Around the vesicles, the mucosa shows inflammatory changes, generally in the form of hemorrhagic cystitis. In the trigonum where the mucosa is more firmly united with the underlying stratum, gaseous vesicles are seen but seldom (STÜRMER, 1937), but microscopy shows that in this situation the gas is localized preponderantly to the tissue spaces of the mucous membrane. Even in the muscularis of the bladder wall, the presence of gas is seen in the tissue spaces. The wall of the individual gaseous vesicles is not lined with epithelium as in cystic cystitis, and the individual vesicles are not in connection with adjacent vesicles. Here and there a vesicle may be seen to contain blood. A small blood vessel is often found to run over a gaseous vesicle. If the wall ruptures, hematuria as well as pneumaturia occur.

There is no *symptom* pathognomonic of emphysematous cystitis, but general bladder symptoms accompanied by the passage of gas on urination is strongly indicative of the presence of emphysematous cystitis. In the few cases described, hematuria occurred in most of them. It must be borne in mind that the passage of gas on urination need not imply that it has been produced in the urinary bladder; it may have entered the bladder by way of a fistula from the intestines or from the genitalia. In 1860 RACIBORSKI (cited by RILEY, 1937) described the first unquestionable, non-fistular case. GUIARD (1883, cited by SØRENSEN, 1910) was the first author to associate pneumaturia with diabetes. In the modern literature, OLSSON (1938) has given a comprehensive account of the occurrence and cause of pneumaturia, together with a description of a spontaneous gaseous pyelogram.

In order to confirm the *diagnosis* of emphysematous cystitis, the presence of gas in the vesical mucosa has to be demonstrated either by cystoscopy or roentgen examination. The appearances presented by emphysematous cystitis on cystoscopy are characteristic. It may be appropriate in this connection to cite LUND et al. (1939):

"Suffice it to say that we who were fortunate to view this condition through the cystoscopic lens were deeply impressed by the picture — the silver sheen reflected from the convex surface of the extremely thin-walled vesicles studding the bladder mucosa, which were rupturing before our eyes and sending bubbles of air toward the dome of the bladder."

Roentgen examination. As is evident from the present case, the roentgenograms vary according to the phase of the disease when the examination is performed. It seems reasonable from the observations made in the present case to distinguish three stages in the amount and location of the gas.

Stage 1: Gas production commences in the bladder wall. On roentgen examination the gas appears as a clear zone, about 1 mm wide, around the contrast medium in the bladder. The gas vesicles are still so small that they cannot be distinguished. The lumen of the bladder is normal and no free gas can be seen in it (Fig. 1).

Stage 2: Gas production in the bladder wall has increased, the latter being irregular, swollen and thicker than before. A great number of gaseous vesicles can now be made out intramurally. The lumen of the bladder has diminished, but contains no gas. There is no pneumaturia (Fig. 2).

Stage 3: Gaseous vesicles have ruptured through the vesical mucosa and free gas is now seen in the bladder. Only a small amount of gas can be demonstrated in the bladder wall. The capacity of the bladder returns to normal (Fig. 3) but later increases in size (Fig. 4). The amount of free gas then gradually decreases and the capacity of the bladder returns to normal again.

In order to be able to distinguish definitely between pneumaturia and an intramural collection of gas, the examinations should always be supplemented with films taken with a horizontal beam projection; by this means, a fluid level will be demonstrated in pneumaturia. But even, with a vertical projection it may be possible to distinguish this condition, since in pneumaturia the free gas collects in the dome of the bladder, whereas intramural gas appears around the contrast medium in the bladder.

Differential diagnosis. Due consideration should be paid to the possibility of gas-filled vesicles that may appear locally in the bladder wall, especially in the trigonum, as a result of the introduction of instruments into the bladder (REDEWILL, 1934). Likewise, the possibility of cystic cystitis should be kept in mind, as this condition cystoscopically may

resemble emphysematous cystitis. Roentgen examination or puncture of a vesicle, however, will establish the diagnosis as the vesicles in cystic cystitis contain no gas but serous fluid.

Course. Most cases of emphysematous cystitis have certainly been first observed on the autopsy table, but in many of these cases the lesion appeared to be an agonal phenomenon and not itself contributory to the death of the patient. There can be no doubt that emphysematous cystitis is a reversible phenomenon, which in most of the cases takes a brief course. Thus ANTOINE (1934) found the changes to disappear on the third day after their discovery. LUND et al. (1939) reported that the gaseous vesicles greatly diminished after three days. MARQUARDT (1940) observed no signs of the lesion after four days, and ORTMAYER (1948), at the end of the same period, found merely insignificant changes in the vesical mucosa. WILHELM (1939) was able in a male diabetic, aged 40, to ascertain a relapse of emphysematous cystitis. The chronologic data cited here refer to cystoscopic findings. As a rule, the complaint of bladder symptoms is of longer duration, which is in harmony with the fact that emphysematous cystitis undoubtedly is merely a phase in the course of an inflammatory process in the vesical mucosa. So far, no instance of chronic emphysematous cystitis has been reported.

Treatment. Even though emphysematous cystitis has a tendency to spontaneous healing, active treatment is still required. This is largely in keeping with the treatment of cystitis in general. Primarily, the gas-producing bacteria should be combated by the employment of the remedies to which they are generally most sensitive — antibiotics. The urinary tract should be examined for primary causes of infections (malformations, calculi, diverticula, tumours). Further, the conditions for gas production by the bacteria should be reduced by bringing a high blood sugar or urinary sugar value to a normal level through dietary measures and the administration of insulin. In addition, the general condition of the patient should be raised. Local treatment by means of instillations has been recommended (*e. g.*, REDEWILL, 1934; LUND et al., 1939), but this was before effective antibacterial remedies had been found.

SUMMARY

A description is given of a case of emphysematous cystitis in a female diabetic, diagnosed roentgenographically and later verified cystoscopically. The changing roentgenographic features observed at the different stages in the course of emphysematous cystitis are pointed out. A brief clinical survey of this rare morbid condition is presented.

ZUSAMMENFASSUNG

Ein röntgenologisch diagnostizierter und später zystoskopisch verifiierter Fall einer emphysematösen Zystitis einer diabetischen Frau wird beschrieben. Das wechselnde

röntgenologische Aussehen, das in verschiedenen Stadien im Verlauf der emphysematösen Zystitis beobachtet wurde, wird hervorgehoben. Ein kurzer klinischer Überblick über diesen seltenen morbiden Zustand wird vorgelegt.

RÉSUMÉ

Description d'un cas de cystite emphysémateuse chez une femme diabétique, diagnostiquée radiologiquement et confirmée plus tard cystoscopiquement. Les modifications des signes radiologiques observés aux différent stades évolutifs de la cystite emphysémateuse sont mises en relief. La clinique de cette affection rare est brièvement esquissée.

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FROM RADIUMHEMMET (DIRECTOR: PROFESSOR A. I. SVEN HULTBERG), STOCKHOLM, SWEDEN

PREGNANCY IN HODGKIN'S DISEASE

by

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In recent Scandinavian literature (SELVAAG, 1952; HENRIKSSON, 1953) induced abortion has been advocated in the case of pregnant women with Hodgkin's disease (H. d.), although general experience tends increasingly to show that pregnancy does not have any unfavourable influence on the course of that disease. Further elucidation of this question therefore seems to be called for — the more so in that pregnancy is apparently not altogether rare in patients with Hodgkin's disease. BICHEL reported pregnancy or pregnancies in 11 of 81 females, including 73 of fertile age: DYES, in 5 of 10; GILBERT, in 11 of 61; HERZ, in 5 of 19; LÜDIN, in 3 of 51; JACKSON & PARKER, in 3 of 82; KASDON, in 3 of 12; and GEMMEL, in 10 of 57, including 39 of fertile age. In the Radiumhemmet series pregnancy or pregnancies occurred in 13 of 100 fertile women. From these figures it is fairly clear that, contrary to earlier assertions, pregnancy is not so rare in Hodgkin's disease. Hence it is so much the more important to know how to act in such cases.

In studying the literature on this subject I have found more than forty papers dealing with H. d. and pregnancy. Over one hundred instances are reported of pregnancies during the course of the disease; 14 of these women have had two or more children. Altogether, these mothers have brought into the world more than a hundred fully healthy children, now aged between one and twenty-five years. Only two women have died while pregnant (BICHEL; PAVIOT, LEVRAT & JARRICOT), and 17 have died within a year after normal delivery. A further four patients have died of the disease one week to six months after induced abortion, which operation has not, therefore, had the desired effect on the course of the disease.

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As regards the children, PRIESEL & WINKELBAUER have described an interesting case in which the disease, they assert, was transmitted from mother to child. The latter died of demonstrable H. d. at the age of about 6 months, and the mother had died of a disease resembling H. d. approximately one month post partum. The autopsy had not, however, revealed unequivocal Hodgkin's disease. This case, therefore, does not provide any conclusive evidence; and indeed several authors have commented sceptically on the aforementioned assertion. LUETKENS has reported the case of a 3-year-old child in whom he observed swollen lymph glands in several regions, and whose mother suffered from "itching"; and VON BRAITENBERG, a case in which a diagnosis of H. d. was made in an infant of only one month whose mother had died shortly after partus. Examination of the placenta, however, had shown no pathologic changes, and it was not established that the mother really had Hodgkin's disease. We possess as yet, therefore, no irrefutable proof that H. d. may be transmitted from mother to child via the placenta. On the contrary, in the great majority of cases the children have been perfectly healthy, and many of them have now reached ages of up to 25 years without any signs of Hodgkin's disease (GILBERT).

There are, it is true, a number of authors who advocate interruption of any pregnancy in women with H. d. (ADAIR; BLITZ; BROWNE; HENRIKSSON; HERZ; HORSTER; LUETKENS; NIKISCHIN; DE PALO; SCHULTZ; SELVAAG), but all of them have observed only one or two personal cases which have had unfortunate courses, and have not been familiar with the relevant literature. Nevertheless they have been guilty of generalisation, which is highly inadvisable in a disease having such a variable course as Hodgkin's disease. GILBERT has repeatedly pointed out that H. d. as a rule is not influenced by pregnancy, and considers that induced abortion is virtually never justifiable in such cases. He has reported 11 patients with H. d. in whom there were a total of 18 pregnancies and 13 children; two of the patients had each had two children, and one of them three. BICHEL holds a similar view, based on experience with 11 personal cases, of which three women each had two children during the course of the disease without any worsening of their condition. One patient died in the seventh month of pregnancy. PAPILLON & CHAVANNE have reported 12 women with H. d. who gave birth to a total of 13 healthy children. Only one of these mothers had died within one year after delivery. KASDON, who describes 3 personal cases and presents an exhaustive review of the papers of fifteen other authors, concludes, similarly, that "there is little evidence from this study to advocate interruption of pregnancy during the course of Hodgkin's disease". A further number of authors subscribe to that view, or consider that each case must be considered separately (FABIAN; GOLDMAN; HEIL-

MEYER; HENNESY & ROFFINO; HEYNEMANN; JACKSON & PARKER; LÜDIN; MOROSI; PALACIOS COSTA *et al.*; PALLASSE *et al.*; PAVIOT *et al.*; PERRIER; VERHAGEN).

The Radiumhemmet Series

Between 1921 and 1952, 373 patients with H. d., including 167 females, were treated at Radiumhemmet. Exactly one hundred of the females were in the 15—45 year age group. Thirteen had one or more pregnancies and, during the course of the disease, gave birth to a total of 19 healthy children, who at the time of writing were aged from one month to 15 years. Some patients had one or more children prior to the onset of H. d., but these children are not included here. One patient is now (July, 1953) in the seventh month of pregnancy. In this group of 13 females there were also four spontaneous abortions. Two pregnancies were interrupted on account of the H. d. and one because of uterine haemorrhages. The age at onset of the disease ranged between 7 and 35 years. Since the case histories contain much of interest, they will be briefly reported.

Case Report

Case 1. No. 2787/38. K. A. J., born 1921. The patient was admitted to Radiumhemmet on Aug. 9, 1938 with fatigue of two years' standing and enlarged cervical glands on the left side. The condition had first been regarded as struma, but biopsy in July 1938 had revealed typical H. d. The roentgen examination of the chest was normal. Roentgen irradiation of the involved glands was prescribed: 8×300 r with 0.5 mm Cu + 1 mm Al filter and 40 cm F. S. D., 175 kV and 7 mA. Intensity: 45 r/min. In December 1938 the patient developed pruritic exanthema over the arms and legs, and was then given roentgen irradiation over the whole body: 5×25 r and 2 m F. S. D. In September 1939 there were enlarged glands medially in the left supraclavicular fossa. The swellings disappeared after teleradium therapy, and the patient has since been quite free from symptoms. She became pregnant in May 1947 and gave birth to a normal child in February 1948. Puerperium was normal. She was again pregnant in September 1952, and was delivered of a healthy girl on June 11, 1953. She was doing her work as a teacher until a week before partus and had not felt so well for years. Puerperium was normal as was lactation. As a matter of fact the patient was not only feeding her own baby but giving 1/2 litre of milk daily to another child as well.

Case 2. No. 6991/39. A. K. O., born 1917. The patient noticed a swelling in the right side of the groin early in May 1939. Biopsy was carried out at another hospital, H. d. being diagnosed. When referred to Radiumhemmet on June 12, 1939, the patient had glands the size of pigeon's eggs in the right groin and the right iliac fossa. Roentgen examination of chest, negative. Subfebrile temperature. S. R. 30 mm. Roentgen irradiation was given from June 12 to 18,1939: Total dose 2,000 r. The patient has since been free from symptoms. Normal pregnancy with partus in March 1944. Spontaneous abortion in the third month, December 1946. *Delivered of twins*, August 1949. None of the pregnancies influenced the patient's condition in the slightest. The puerperia were uneventful and lactation caused no difficulties.

Case 3. No. 7963/39. A.-L. O., born 1924. Increasing fatigue in the winter of 1938 and following spring. In June 1939, enlarged glands were observed in the left supraclavicular fossa. Biopsy was carried out at another hospital, the pathologic diagnosis being typical H. d. When admitted to Radiumhemmet on July 21, 1939, the patient had several involved lymph glands on both sides of the neck and in the left supraclavicular fossa. Roentgen examination of chest, negative. Roentgen irradiation was given from July 21 to Aug. 5, 1939. Total dose 1,900 r to both sides of the neck. The patient was thereafter free from symptoms. Normal pregnancy with partus in May 1948; likewise February 1952. There was no influence on the disease. Puerperia and lactation were normal. The children, now aged 5 and 1 year respectively, are both healthy, and the mother is symptom free.

Case 4. No. 9473/39. B. K. H., born 1913. The patient became pregnant in January 1938, and during the ensuing spring had an increasing swelling anteriorly in the neck. It was first regarded as a struma, and general roborant therapy alone was prescribed. Partus occurred on October 27, 1938 and, like the puerperium, was fully normal. There was an exacerbation in the following spring, with several enlarged glands bilaterally in the neck and supraclavicular fossae. Biopsy at another hospital in September 1939 showed typical H. d. On admission to Radiumhemmet, Oct. 9, 1939, there was involvement of the mediastinal glands too. S. R. 52 mm. Fever. Anemia. Roentgen irradiation was given to both sides of the neck and to the mediastinum in a total dose of 2,100 r over each field. In May and September 1940, supplementary series were given to the mediastinum, where the glands still showed some enlargement. Thereafter the patient was free from symptoms. There was a further pregnancy in 1945, with normal course and partus in January 1946. The patient remained symptom free till April 1949, when bronchopneumonia developed. Her condition worsened in February 1950, with cough, fatigue and loss of weight, a roentgen examination disclosing parenchymal infiltrations in the lungs. These were treated by roentgen irradiation from one large anterior and one posterior field: 8×50 r to each, with 0.5 mm Cu and 1 mm Al filter; 80 cm F. S. D.; 170 kV and 15 mA. The condition slowly improved. Supplementary treatment was given in May 1950, with 4×50 r to each of the two fields. Thereafter there was a continuous improvement, and since October 1950 the patient has been symptom free. The children, now aged 15 and 7 respectively, are healthy.

Case 5. No. 9857/43. A. K., born 1907. Noticed enlarged lymph glands in the left supraclavicular fossa in 1938. They considerably increased during pregnancy in 1940, but diminished spontaneously after partus. Pregnancy, partus and puerperium were normal. Later there were sporadic attacks of fever over a period of some months. Further pregnancy in 1941, with a normal course, partus and puerperium. Increasing fatigue and loss of weight (7 kg) in 1942, the glands again increasing in size. Biopsy in May 1943 showed typical H. d., and roentgen examination disclosed enlarged glands in the mediastinum. Admitted to Radiumhemmet in May 1943 and received roentgen irradiation: 6×400 r to each situation. In the next few years there were symptom-free periods alternating with periods with enlarged glands of varying situation and occasional spells of fever and pruritus. Roentgen irradiation was given to the glands. In January 1948 there was persistent high fever and a large infiltration in the right lung. Antibiotics for two weeks had no effect; on the contrary the pulmonary lesions increased in size and the fever was unchanged. Nitrogen mustard therapy was then resorted to, with exceptionally good results. During the ensuing years roentgen irradiation was given to fresh foci, and nitrogen mustard in 1949 and 1951 on generalisation of the disease. Further biopsy in November 1951 gave the same diagnosis as before. The pa-

tient is at present in good general condition, but is occasionally distressed by pruritus. Her children, now 13 and 12 respectively, are both healthy.

Case 6. No. 4505/45. G. E. S., born 1918. Fell ill in December 1944 with fever, fatigue and loss of weight. In January 1945, enlarged glands were observed in the left supraclavicular fossa. Roentgen examination revealed large glands in the mediastinum. Biopsy at another hospital in February 1945 showed typical H. d. S. R. 65 mm. The patient was admitted to Radiumhemmet on Feb. 26, 1945 and received roentgen irradiation to the mediastinum in a total 'tumour dose' of about 2,300 r. She became pregnant in July 1945 and since the disease was in an active stage, the then senior physician advised abortion, which was performed on Oct. 16. The placenta and fetus showed no signs of H. d. However, there was no demonstrable influence on the course of the disease, either by the pregnancy as such or by the induced abortion. Further roentgen treatment was given in March 1946: 6 × 400 r to glands in the right supraclavicular fossa. When the patient again became pregnant in February 1947, it was not interrupted, but spontaneous abortion occurred on June 18, 1947. Neither the patient's condition nor the disease were affected. There were subsequently a further two pregnancies in 1948 and 1952, both fully normal; and both patient and children, now 5 and 1 year respectively, are at present healthy.

Case 7. No. 4508/45. H. I. M. S., born 1921. Previously healthy. Abortion (probably spontaneous) in the third month, in October 1943. In December 1943, there were incipient attacks of dyspnoea and cough, which were aggravated at the time of menstruation. Later, enlarged cervical lymph glands were observed. In April 1944 one gland was removed for microscopic examination at another hospital and disclosed H. d. of malignant type. Roentgen examination of chest, negative. Roentgen irradiation was given, but in a total dose of only 800 r. The patient was not referred to Radiumhemmet till February 1945, when she again showed enlarged cervical lymph glands bilaterally and was in the third month of pregnancy. The then senior physician recommended immediate abortion and sterilisation. The placenta and fetus presented no signs of H. d. Roentgen irradiation was given from March 12 to 22, 1945: 6 × 400 r to the right side of the neck but only 5 × 300 r to the left side, which had been irradiated previously. The general condition improved and the swellings subsided. Neither pregnancy nor abortion could be said to have influenced the course of the disease. An exacerbation occurred in January 1947, with large glandular bundles in the mediastinum, which were treated by roentgen. Generalisation occurred in March 1948, nitrogen mustard gas being given in May. Thereafter there was a general improvement; the patient remained symptom free and fit for work till the spring of 1950, when *pulmonary tuberculosis* was detected; this progressed and the patient died in May 1951.

Case 8. No. 6261/46. E. L., born 1920. The disease was ushered in with pruritus and enlargement of the left axillary lymph glands in 1939. Roentgen irradiation in small doses was given at another hospital. Following a recurrence in 1940 a group of glands was extirpated in the axilla, but unfortunately no microscopic examination was carried out. The patient became pregnant in 1943, with normal partus in the autumn of 1944, puerperium and lactation being uneventful. In December there were enlarged glands in the left supraclavicular fossa as well as periodic fever. Roentgen irradiation was given in January 1945, but again with inadequate doses, so that the swellings never fully subsided. Severe pruritus and loss of weight supervened in January 1946. This was at first regarded as scabies by a physician, but biopsy of a gland in March 1946 showed typical H. d. On admission to Radiumhemmet, March 27, 1946, the patient had lost further weight and was anaemic. S. R. 92 mm. Fever. Enlarged glands were found in

both supraclavicular fossae and in the left inguinal region. The spleen too was enlarged. Adequate roentgen therapy brought about a considerable improvement and the weight rose by 8 kg. During the ensuing years there were periods of exacerbation and generalisation. Nitrogen mustard was given in March and December 1948 and July 1949. A further serious exacerbation in January 1950 was treated by various forms of therapy without any effect, the patient dying in April 1950. The child, now 9, is healthy.

Case 9. No. 10405/46. G. D. Ö., born 1906. Normal pregnancy and partus in 1936 and again in 1939. The patient fell ill in June 1941 with periodical fever, cough and high S. R. The symptoms disappeared when she became pregnant in the autumn of 1941. Pregnancy ran a normal course; the patient felt quite fit and was delivered of a healthy child in the summer of 1942. Puerperium and lactation were uneventful. In the spring of 1943 there was a recurrence of the same symptoms; in addition, pruritus supervened and grew in severity. In January 1944, enlarged mediastinal lymph glands were observed; they received roentgen treatment at another hospital with small doses in February, May and November 1944. Arsenic treatment followed in the autumn of 1945, as well as tentative Grenz ray therapy for the pruritus, though without effect. On admission to Radiumhemmet, June 3, 1946, the patient had severe pruritus, fever, and enlarged glands in the mediastinum and parenchymal infiltrations in both lungs. In addition there was a large group of involved glands in the epigastrium. In view of all the previous roentgen series with inadequate dosage, only a focal dose of about 1,000 r could now be applied. (At that time nitrogen mustard had not yet been tried therapeutically at Radiumhemmet.) The patient died on Aug. 22, 1946. Her child, now 11, is healthy.

Case 10. No. 18202/47. M. H. H., born 1910. Became ill in 1941 with abdominal pain. At another hospital she underwent resection of about 50 cm of the small intestine for a tumour formation. Pathologic diagnosis was typical H. d. involving both intestinal wall and lymph glands. During the next year or so incipient ileus occurred twice, and in January 1943 led to further laparotomy, the findings being negative. Normal pregnancy and partus in 1944, and a spontaneous abortion in 1945. The patient again became pregnant in 1946 and was delivered of a healthy child at full term. Puerperium and lactation were fully normal on both occasions. There was a recurrence of severe abdominal pain and moderately elevated temperature in October 1947. Since the symptoms became alarming, a third laparotomy was performed, disclosing a recurrence at the anastomosis site as well as a number of infiltrations in the small bowel, enlarged glands in the abdomen, and a large infiltration in the posterior surface of the uterus. The old anastomosis was resected and a number of glands in the mesenterium extirpated. Pathologic diagnosis: Typical H. d. Roentgen examination of chest, negative. The patient was now referred to Radiumhemmet, and admitted there on Dec. 15, 1947. Roentgen irradiation was given over the entire abdomen through four anterior and two posterior fields between Dec. 15, 1947 and Jan. 20, 1948: 1,800 r to each field; 0.5 mm Cu and 1 mm Al filter; 60 cm F. S. D. There was a considerable improvement, but the patient became ill again in June 1948 with loss of weight, fatigue, diarrhoea and dull abdominal pain. High S. R. and fever, so that nitrogen mustard was administered from Sept. 15 to 18, 1948 with an exceptionally good effect. In the next six months the weight rose by 8 kg. The patient has since been free from symptoms, and her children, now 9 and 7 respectively, are healthy.

Case 11. No. 4403/51. B. F., born 1922. Previously healthy and with two healthy children. The onset occurred in the spring of 1951, with loss of weight and tiredness, in May the patient observing enlarged glands in the left axilla. Fever supervened

in June. Biopsy of the glands at another hospital showed a "malignant tumour of sarcomatous type". Since the patient had had irregular uterine haemorrhages from April 1951, curettage of the uterus was performed on July 3, 1951 and disclosed a fetus in the second to the third month. Neither placenta nor fetus presented any signs of disease. The patient was admitted to Radiumhemmet on July 30, 1951, and then had a number of enlarged lymph glands in the left axilla, left supraclavicular fossa and left side of the neck. Anaemia; Hgb 48 per cent. A further biopsy showed unquestionable H. d., and the patient was given blood transfusions and roentgen therapy; the latter in doses of only 75 r initially, but increasing to 300 r daily as the general condition improved. The total dose in the glands was 2,325 r. During the autumn other glandular regions became involved and were treated. In April exacerbation and generalisation occurred, wherefore nitrogen mustard was given from April 22 to 25. Following a rapid improvement the patient remained symptom-free till the middle of September 1952. Further therapy had little effect, and she died in January 1953. Neither pregnancy nor abortion can be held to have influenced the course.

Case 12. No. 4776/51. A.-L. R., born 1931. At the age of 7—8 years there had been enlarged glands in the neck, axillae and groin. The condition improved after general roborant therapy, but a small glandular mass persisted in the right supraclavicular fossa. Normal pregnancy and partus in 1946. Early in December 1950 the glands grew in size and further enlarged glands appeared in the mediastinum. Biopsy was carried out at another hospital on Dec. 15, 1950, H. d. being diagnosed. Roentgen therapy was given. On admission to Radiumhemmet, Aug. 17, 1951, the patient was in the second month of pregnancy. Between Aug. 21 and Sept. 14, she received roentgen irradiation of the mediastinal lymph glands in a 'tumour dose' of about 2,400 r. Pregnancy proceeded normally, but in March 1952 a glandular mass developed at the angle of the jaw on the right side. It was treated by roentgen in a total dose of 2,100 r. A healthy child was delivered on April 8, 1952, puerperium and lactation being uneventful. Between June 13 and 18, 1952, supplementary teleradium was given to the remains of a gland in the right supraclavicular fossa. In November there were pruritus and enlarged glands in the right axilla, the region being irradiated. Thereafter the patient was symptom-free and fit for work till June 1953, when new glandular regions became involved and the pruritus returned. Nitrogen mustard was then administered with good effect. Both children, now 7 and 1 year respectively, are healthy.

Case 13[1]. No. 7297/51. B. N., born 1917. Bipara. Operated on for thyroid adenoma in 1947 and for adenoma of the left breast in January 1952. In the spring of 1952 there were several periods of fever up to 40° C and pain in the chest and back. The patient sought treatment at another hospital, but no diagnosis could be established. She was admitted to Karolinska Sjukhuset, where a roentgen examination on Oct. 1, 1952 revealed a glandular density the size of a fist in the upper mediastinum. Anaemia. S. R. 101 mm. Since the diagnosis still had not been established, roentgen therapy was given cautiously between Oct. 6 and 23: Total dose 1,000 r over each of four fields to the mediastinum. Follow-up roentgen examination on Dec. 16, 1952 showed a normal mediastinum, and the S. R. was 13 mm. In January 1953 the patient was found to be in the second to third month of pregnancy; she then had a palpable lymph gland in the right supraclavicular fossa. It was removed for microscopic examination and showed typical H. d. Roentgen therapy was given with good results, and the patient is now (July 1953) in excellent condition. The pregnancy is following a normal course.

[1] Case 13 was Sept. 13, 1953 delivered of twins. Puerperium and lactation were fully normal. Mother and children are in good condition.

Of the 13 women 9 are still alive and well, 8 of them from 8 to 15 years, and one 1 ½ years after the onset of the disease. Unequivocal microscopic diagnoses were obtained in all these cases. (The preparations have been re-examined by Radiumhemmet's pathologist.) One patient (Case 8) died 6 years after partus and 11 years after the onset of H. d., and one (Case 9) 4 years after normal pregnancy and partus, and 5 years after the onset of H. D. Thus, none of these women died in connection with pregnancy, or even within a year after it. The case with the most unfortunate course concerned one of the patients who underwent induced abortion (Case 11). I am in no way suggesting, however, that this induced abortion was responsible for the outcome; rather the pregnancy was doubtless interrupted because the patient was deemed to be in poor condition, with H. d. in an active phase. In none of our cases has an induced abortion caused any improvement in the course of the disease.

In the above-mentioned patient (Case 11) who underwent induced abortion, the condition did not improve after the operation; the woman died 1 ½ years later, 2 years after the onset of the disease. One patient (Case 6) had her first pregnancy interrupted about 6 months after the onset of H. d.; she later had a spontaneous abortion, and has since given birth to two healthy children. In the third case (Case 7) induced abortion had been resorted to twice, together with sterilisation on the second occasion. The patient's condition was not improved, however, by these measures; on the contrary there were continual exacerbations during the ensuing years and she seldom felt really well, notwithstanding roentgen treatment, blood transfusions and chemotherapy. She ultimately died 6 years after the last abortion. In her case, however, the disease was complicated in the later stages by coexistent pulmonary tuberculosis.

Four of the patients (Cases 1, 8, 9 and 13) said they had never felt so well as they did during the pregnancies — an observation noted also by other authors (Bichel; Morosi). Another patient (Case 4), on the other hand, had an exacerbation during the first pregnancy, with a spontaneous improvement after partus; but she was quite well during the second pregnancy 7 years later. In the other cases no influence on the patients' lymphogranulomatosis was detectable, and both pregnancy and partus showed normal courses.

Women with H. d. who become pregnant during a remission of the disease generally do best, according to both Bichel and Gilbert and others. The prognosis appears to be poorer for those who become pregnant either during an active progressive phase, or are pregnant when the disease has its onset (Gilbert; Papillon & Chavanne).

Normal pregnancy and partus occurred in 8 of our patients during

symptom-free intervals (Cases 1, 2, 3, 5, 8, 10, 12 and 13). These mothers gave birth to a total of 15 healthy children, including one set of twins. Puerperia and lactation too were quite normal. Seven of the mothers are still in good health — six of them 12 to 15 years and one 1 1/2 years after the onset of the disease. One woman died 6 years post partum and 11 years after the initial symptoms of H. d. had appeared.

Only in one patient (Case 4) did the onset of lymphogranulomatosis coincide with pregnancy. Enlarged cervical lymph glands were observed in the third to fourth month of pregnancy. The disease was kept under control by roentgen therapy, and both the first pregnancy and a further one 5 years later showed normal courses. Both children and mother are now alive and well, 15 years after the onset of H. d. — which fact is exceedingly noteworthy in view of the poor prognosis that has been assigned precisely to such cases in the literature.

The remaining four patients became pregnant while the H. d. was in an active phase. Only one of them (Case 6) is still alive — 8 years after the onset of the disease — but she has had two abortions and two normal pregnancies with healthy children, now aged 5 and 1 year respectively. One patient (Case 11) died 1 1/2 years, and one (Case 7) 6 years after induced abortion. The fourth (Case 9) died 4 years post partum, and at no time during those years was it possible to bring about a complete remission of her symptoms. Yet in none of these four women is there the slightest evidence that the H. d. was aggravated by pregnancy or that the course was changed by the abortions.

Therapy

I would emphasise here, as GILBERT has consistently done in his papers, the importance of adequate roentgen therapy. We have accordingly given total 'tumour doses' amounting to at least 2,000 r, and often more. The daily dose, having regard to the patient's general condition, etc., has varied between 100 and 400 r, measured on the skin. The irradiation has been given with 165—180 kV and 10—20 mA; 0.5 mm Cu + 1 mm Al filter; 40—60 cm F. S. D., and an intensity of 25—50 r per minute. The aim has been *to destroy accessible lymphogranulomatous foci completely, as far as possible with the first series.* The repeated local recurrences in patients who had received, at other clinics, what in our view were unduly small doses (800—1,000 r) has lent added weight to our opinion as to the correctness of this principle of treatment (Cases 7, 8, 9 and 12). Moreover, only in extremely rare instances have we ourselves observed recurrences in the same glandular region following adequate radiation series.

Nitrogen mustard has been resorted to only on generalisation of the disease, and never of course during pregnancy. Further, patients who have undergone nitrogen mustard therapy should doubtless be strongly advised against pregnancy, since that agent, like other radiomimetic substances and radioisotopes, may cause damage to the ovaries, with consequent risk of genetic defects in future offspring.

Conclusions

On the basis of the literature and personal experience, the following conclusions may be drawn.

1. Pregnancy is not uncommon during the course of Hodgkin's disease.
2. From the obstetric point of view there is no reason to interrupt pregnancy in that disease; for pregnancy, partus and puerperium run a normal course.
3. There is no evidence that exacerbations are more common during pregnancy than otherwise.
4. There is no conclusive proof that H. d. may be transmitted from mother to child via the placenta; on the contrary, the great majority of children are healthy, and in some cases have been followed up until reaching adult age.
5. Only in a few exceptional cases is it justified to interrupt pregnancy in Hodgkin's disease, namely:
   (a) where complicated by tuberculosis or some other disease;
   (b) where the general condition is so badly affected that death of the mother may be feared before full term, so that no possibility of saving the child can be expected;
   (c) where the disease is localised to the inguinal or pelvic regions, making roentgen treatment impossible having regard to the risk of radiation damage to the fetus;
   (d) where the mother has previously undergone treatment with nitrogen mustard or other radiomimetic substances (due to the risk of genetic damage).
6. Lactation may be permitted if the patient is in good condition and does not require radiation treatment; it should otherwise be withheld or, for the sake of the child, possibly allowed tentatively for the first two to three weeks.

SUMMARY

During the period 1921—1952 a total of 373 patients with Hodgkin's disease, including 167 females, were treated at Radiumhemmet. Exactly one hundred of the females were aged between 15 and 45, and 13 of these had one or more pregnancies and

gave birth to 19 healthy children. In addition there were four spontaneous and three induced abortions. In no case does pregnancy appear to have caused any acute exacerbation of the disease. The cases are briefly reported. Eight of the patients are alive and in good health 8—15 years after the onset of the disease. None died in connection with pregnancy or within a year after delivery. Pregnancy, parturition and puerperium ran normal courses from the obstetric point of view. From this experience as well as over a hundred cases reported by various authors, the writer considers that there is seldom any indication for interruption of gravidity in patients with Hodgkin's disease.

ZUSAMMENFASSUNG

In dem Zeitraum von 1921 bis 1952 wurden im Radiumhemmet in Stockholm insgesamt 373 Patienten mit Hodgkinscher Krankheit behandelt; von diesen waren 167 Frauen. Genau 100 Frauen waren zwischen 14 und 45 Jahre alt; 13 der Frauen waren einmal oder mehrmals schwanger und wurden von 19 gesunden Kindern entbunden. Ausserdem lagen 4 spontane und 3 provozierte Aborte vor. In keinem Falle scheint die Schwangerschaft eine akute Verschlimmerung der Krankheit hervorgerufen zu haben. Die Fälle werden kurz wiedergegeben. Acht Patienten leben in bester Gesundheit 8—15 Jahre nach dem Auftreten der Krankheit. Kein Patient starb während der Schwangerschaft oder innerhalb eines Jahres nach der Entbindung. Schwangerschaft, Entbindung und Puerperium hatten einen vom obstetrischen Gesichtspunkt normalen Verlauf. Auf Grund dieser Erfahrungen sowie auf Grund von über 100 von verschiedenen Autoren berichteten Fällen ist der Verf. der Ansicht, dass es selten indiziert ist, eine Schwangerschaft bei Patienten mit Hodgkinscher Krankheit zu unterbrechen.

RÉSUMÉ

Pendant la période 1921—1952 un total de 373 malades atteints de maladie de Hodgkin, dont 167 femmes, ont été traités au Radiumhemmet. Cent femmes exactement étaient âgées de 14 à 45 ans, et parmi elles, 13 ont eu une ou plusieurs grossesses et ont donné naissance à 19 enfants en bonne santé. Il y eut de plus quatre avortements spontanés et trois provoqués. Dans aucun cas la grossesse ne semble avoir causé d'exacerbation aiguë de la maladie. Les cas sont brièvement présentés. Huit des malades sont en vie et en bonne santé 8 à 15 ans après le début de la maladie. Dans aucun cas la mort n'est survenue du fait de la grossesse ou dans l'année qui a suivi l'accouchement. Du point de vue obstétrical la grossesse, l'accouchement et les suites de couches se sont déroulés normalement. De cette expérience et de plus de cent cas publiés par divers auteurs, l'auteur conclut qu'il est rarement indiqué d'interrompre une grossesse chez les malades atteintes de maladie d'Hodgkin.

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FROM RADIUMHEMMET (DIRECTOR: PROFESSOR SVEN HULTBERG), STOCKHOLM, SWEDEN

THE TREATMENT OF PLASTIC INDURATION OF THE PENIS (PEYRONIE'S DISEASE)

by

Olov Dahl

Plastic induration of the penis, or Peyronie's disease, is a condition characterized by fibrous induration of the intercavernous septum and/or of the tunica albuginea of the penis. It results in the formation of plaques of varying size, form, consistency, and location. The disease usually appears in middle age. The principal symptoms that may occur are penile curvature on erection, pain on erection, and disturbances of coitus.

The methods of treatment most frequently used are roentgen and radium irradiation, surgical removal of the plaques, and adminstration of vitamin E. Surgical treatment has not earlier brought any major success, and though the application of modern methods of plastic surgery has afforded in the past few years some hope of better results, no large series of cases thus treated have yet been published. In this paper only the non-surgical methods of treatment will be discussed, the purpose being to give a description and a critical appraisal of these methods on the basis of Radiumhemmet's series and of the available literature.

The present investigation opened with the vitamin E treatment of a series of cases at Radiumhemmet. To secure a comparative series I later studied the cases irradiated at Radiumhemmet during the preceding eleven-year period. The criteria of evaluation will therefore be understood best if we first consider the vitamin E method, even though it is the most recent of the non-surgical methods of treatment.

Treatment with Vitamin E

SCOTT and SCARDINO (1947), prompted by reports of partially successful treatment of certain connective tissue diseases with vitamin E, tried

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that agent in a series of cases of plastic induration, and in two papers communicated relatively good results. Since then certain authors (WIJNBLADH; KATZ-GALATZI; STEINBERG, 15; NIKOLOWSKI; AURIG and SÜSSE) have each reported partially satisfactory results in a relatively small number of cases treated.

The mechanism of action of vitamin E in such cases is not known in detail. Those investigators who have studied these problems seem inclined to accord vitamin E a rôle in the maintenance and in the restoration of the normal morphology of collagenous connective tissue and of the small blood vessels (for reviews, *vide* MARKEES and STEINBERG (15)).

In 1949 this method of treating plastic induration was taken up for clinical trial at Radiumhemmet. In order, as far as possible, to avoid selection, all untreated cases admitted to Radiumhemmet during the period from October 1949 to December 1950 were included. But since the disease is comparatively rare, this series comprises only fourteen cases. In order to obtain the largest possible series within a relatively short time, certain of the previously irradiated cases which underwent routine checks during the period in question, were included. Those cases were selected in which the radiation treatment had been followed by no or only moderate improvement, and in which no progressive improvement in the preceding six months had occurred. The age incidence in the total series, comprising eighteen cases, will be seen from Diagram 1.

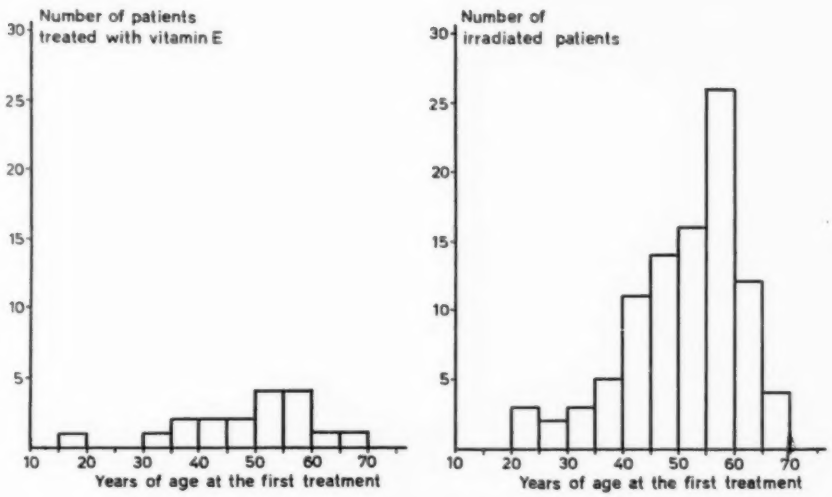

Diagram 1.

Two types of vitamin E preparations are available. Natural vitamin E preparations contain alpha-, beta-, gamma-tocopherol, and sometimes, in addition, delta-tocopherol. The potency of such preparations, usually called mixed tocopherols, is defined in terms of their equivalence to synthetic alpha-tocopherol. Other vitamin E preparations contain synthetic alpha-tocopherol. Those used in the present investigation consisted mostly of mixed tocopherols and to a lesser degree, of synthetic alpha-tocopherol.

Mixed tocopherols in the form of 'E-vimin forte' were supplied by AB Astra, Södertälje, Sweden as 'Concentrated wheat germ oil, containing vitamin E equivalent to the biologic action of 50 mg dl-alpha-tocopherol per capsule'.

Synthetic alpha-tocopherol in the form of 'Ephynal forte' was supplied by Hoffman-La Roche AB, Stockholm, in 'Tablets containing 50 mg dl-alpha-tocopherol acetate'.

Mixed tocopherols were used alone or almost exclusively in nine cases. In the other nine, synthetic alpha-tocopherol was administered for the first third, on the average, of the period of treatment, and mixed tocopherols thereafter. The choice at different times and in different cases was determined solely by the supply of the respective preparations.

STEINBERG (15) observed that his study "does not indicate the superiority of fortified tocopherols as compared to the regular mixed natural tocopherols". The present series has not shown any demonstrable superiority of either preparation.

In accordance with the view of previous authors regarding the approximately optimal dose, I administered 300 mg by mouth daily. No untoward effects were observed. This finding accords with the experience of earlier authors (SCOTT and SCARDINO, KATZ-GALATZI, STEINBERG). NIKOLOWSKI, however, claims to have demonstrated that in partially damaged spermiogenesis, vitamin E in high dosage may cause progression of the damage, and he recommends controls of the ejaculate.

The treatment was continued as long as a distinctly progressive improvement could be observed, though for at least six months. The longest duration of treatment was seventeen months and the average nine months. In four cases radiotherapy was given immediately after the conclusion of the vitamin E treatment. The other cases were followed up for at least seven months after the cessation of treatment, most of them considerably longer.

To facilitate uniform evaluation, I, myself, carried out both the primary and the follow-up examinations. Besides particulars furnished by the patients, the evaluation must be based on a single sign, namely, the character of the penile plaques. To secure as high a degree of uni-

formity as possible notwithstanding these difficulties, a grading system was devised. In accordance with the principles of the latter, of which space does not permit a detailed description, it was possible to grade each of the symptoms — penile curvature, pain on erection, and disturbances of coitus, as well as the sign of penile plaques, according to the scale: 'not present', 'moderate', 'marked' and 'severe'. Further, it was possible to grade any change in a symptom or sign in conjunction with treatment according to the scale: 'disappearance', 'marked decrease', 'moderate decrease', 'no change' and 'increase'. On the basis of these grades, the result in each case was then classed as: 'pronounced improvement', 'moderate improvement' or 'poor result'. The grade 'pronounced improvement' was used only if almost complete or complete recovery had occurred, and this recovery had to include a marked objective decrease or total disappearance of the induration. Cases showing very slight improvement or none at all were graded as 'poor results'. In grading, account was taken of any change of the condition that may have occurred during the follow-up period after cessation of therapy.

The following case reports exemplify the use of the grading system and, above all, the principles for grading of the results.

Case No. 11232/1950.

Tocopherol treatment for 7 months, beginning at 54 years, 2 months after onset of symptoms.

Symptoms and sign	Pre-treatment state	Post-treatment state
Penile curvature	Marked	Marked decrease
Pain on erection	Moderate	Disappearance
Disturbances of coitus	Moderate	Disappearance
Penile plaques	Severe	Marked decrease

A further decrease of penile curvature and penile plaques was found 9 months after cessation of therapy.

Result: Pronounced improvement.

Case No. 9664/1950.

Tocopherol treatment for 7 months, beginning at 54 years, 6 months after onset of symptoms.

Symptoms and sign	Pre-treatment state	Post-treatment state
Penile curvature	Moderate	No change
Pain on erection	Moderate	Marked decrease
Disturbances of coitus	Marked	Moderate decrease
Penile plaques	Severe	Moderate decrease

No further change was found 16 months after cessation of therapy.

Result: Moderate improvement.

Case No. 13253/1947.

Tocopherol treatment for 10 months, beginning at 66 years, 2 months after onset of symptoms.

Symptoms and sign	Pre-treatment state	Post-treatment state
Penile curvature	Severe	Increase
Pain on erection	Moderate	Disappearance
Disturbances of coitus	Marked	No change
Penile plaques	Marked	Moderate decrease

No further change was found 10 months after cessation of therapy.
Poor result.

In the present series the initial symptoms had been observed between one and fifty-nine months — on the average, just under thirteen months — before the institution of vitamin E treatment. In seventeen cases penile curvature was present from the outset. It disappeared under treatment in two cases and showed a decrease in four. Pain on erection was present in thirteen cases; it disappeared in six and decreased in four. Disturbances of coitus, which had been present before therapy in thirteen cases, had disappeared after treatment in four and decreased in three. Pain on erection was accordingly the symptom that responded to treatment most frequently and most markedly. Lastly, the sign of penile plaques was present in all cases; it disappeared in three and showed a marked and a moderate decrease in two and five cases respectively. As a general rule, it was the symptom of pain on erection that commenced to abate first.

Four of the present cases showed 'pronounced improvement', six 'moderate improvement', and eight 'poor result'. Five patients showed a subjective improvement of the general condition, both physical and mental, in conjunction with treatment.

Radiation Treatment

In the nineteen-twenties and 'thirties a small number of cases with plastic induration were treated at Radiumhemmet with the teleradium apparatus designed by SIEVERT and by surface application of radium tubes in moulds (dental compound) according to EDLING's method. However, not only was the use of such methods troublesome in Peyronie's disease, but it was also difficult to compute there with sufficient accuracy the doses received. This difficulty was reflected in the fact that some cases showed persistent changes due to radiation in the form of extensive teleangiectasis, atrophic skin with a tendency to ulcerate, or slight symptoms of urethritis. It constituted a considerable improvement of

the technique when, about 1940, on the initiative of STRANDQVIST, Radiumhemmet started to use in Peyronie's disease his method of surface application of radium tubes in glass capsules; and likewise when, around the same time, fractioned roentgen irradiation commenced to be employed in suitable cases. For since both methods permit doses to be calculated with satisfactory accuracy, it was possible to control the dosage and, with mounting experience, to adapt it to the requirements of the disease and to the tolerance of the tissues.

The experience thus acquired at Radiumhemmet in the nineteen-forties has led to the principles of therapy that will now be described.

In relatively superficial and circumscribed indurations, radium treatment is resorted to. It consists in the use of radium tubes containing eight milligrams of radium and placed in glass capsules, which are fixed parallel to each other in one or two rows. STRANDQVIST, in two papers, has described the method in detail. The number of tubes and rows depends on the size and shape of the indurations. The total number of tubes required, applied in two rows, is never likely to exceed thirty. Moreover, roentgen treatment should be the method of choice whenever the indurations are fairly extensive and involve the deeper tissues. The tubes, when applied in two rows, are placed in 'roof-truss' formation as shown in Figure 1.

Fig. 1.

In this form of radium therapy, the dose is taken as the average of that from the surface to a depth of one centimeter. This conception was introduced by STRANDQVIST (16), who demonstrated that according to clinical experience it is associated with conformity between doses and skin reactions — which is desirable in a method designed for treatment of diseases situated at or near the surface. The duration of treatment required with any given applicator, corresponding to the desired 'average dose', is computed in accordance with STRANDQVIST's directions (16). We nowadays take, however, a value of 8.3 r per hour as the dose rate equivalent to 1 Imc unit and not the earlier value of 7.5 r per hour (earlier doses mentioned in this paper are corrected accordingly).

Roentgen irradiation is invariably resorted to if the indurations

involve the deeper layers or are fairly extensive, as well as in all indurations situated in the perineal parts of the corpora cavernosa. The treatment is given with a filter of 0.5 mm Cu and 1.0 mm Al and at a tension of 170 kV, corresponding to a HVL of about 0.9 mm Cu; focus skin distance 40 cm; tube current 15 mA; dose rate (measured on the skin) 85 r per minute with a field of 20 sq. cm.

Studies of the distribution of doses carried out in conjunction with this investigation showed that the doses in the deeper lying tissues of the penis are two to three times greater with roentgen than with radium treatment. Hence, there is ample justification, physically, for the aforementioned principle of using roentgen rays for indurations situated in the deeper layers. The computations of doses in the above mentioned studies were carried out by Dr. S. BENNER at the Institute of Radiophysics, Stockholm (now at the Radiophysics Laboratory, Gothenburg).

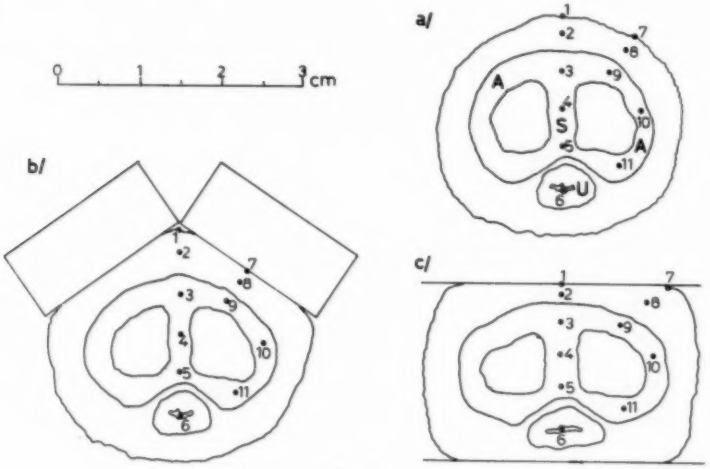

Fig. 2.

Fig. 2 a shows a cross-section of the corpus penis — schematic representation after SOBOTTA, 1911. *A* denotes the tunica albuginea, *S* the intercavernous septum, and *U* the urethra. Fig. 2 b shows the same organ with 'roof-truss' placed radium applicators and the change of form caused by them. Fig. 2 c depicts roentgen treatment under compression.

In the following tabulation the two forms of treatment are compared with respect to the doses at points 1 to 11. In each instance the dose at point 1 is taken to be 100. (In each case the field has a length of five centimeters; with radium treatment this corresponds to twenty tubes, applied in two rows. The same comparison with fields having a length of 2.5 and 7.5 cm respectively — the equivalent of 2×5 and 2×15 radium tubes — shows a similar ratio between radium and roentgen doses.)

Point	1	2	3	4	5	6	7	8	9	10	11
Radium	100	80	58	43	33	23	96	79	62	39	27
Roentgen	100	99	95	92	87	77	92	94	90	87	80

Empirically, an 'average dose' of 1,100 r has been found to be appropriate in radium treatment.

In the great majority of cases two rows of tubes, applied in 'roof-truss' formation, were used. The prescribed 'average dose' was certainly in the neighbourhood of 1,000 r. To facilitate calculation of the duration of treatment required, however, the angle formed by the applicators was not generally taken into account. For this reason the majority of cases in the present series must have actually received a higher 'average dose' than that prescribed — according to present calculations, approximately 1,100 r.

In roentgen treatment, the usual skin dose (back scatter included) is 1,200 r from one direction or 750 r from each of two opposite directions, in each case fractionated over three days.

From clinical experience the radium and roentgen methods of treating plastic induration of the penis, used on correct indications and with conventional doses, are roughly equivalent as to both the cutaneous reactions and the curative effect. It is thus interesting to observe that the 'average dose' values in the two forms of treatment are, according to present calculations, approximately the same. (The radium treatment is considerably more protracted, but on the other hand the roentgen dose is fractionated over three days.) STRANDQVIST (17) called attention to similar conditions in radiation treatment of cavernous hemangiomas. The conventional skin dose of radium (computed for application of twenty tubes in two rows and an 'average dose' of 1,100 r), on the other hand, is scarcely 1,600 r, *i. e.*, about 30 per cent higher than the customary skin dose of roentgen rays.

Experience shows that supplementary treatment, if required, following primary radium therapy should be given after six months at the earliest. If radium be chosen again, the 'average dose' should not exceed 600 r. Since an unsatisfactory effect of the initial radium treatment might be due to changes in the deeper layers of the penis as well, roentgen rays were often chosen for supplementary treatment, and this was found to be beneficial. The skin dose should not exceed 900 r, fractionated over three days.

Any supplementary treatment following primary roentgen therapy should, in our experience, be after an interval of at least three months; the skin dose should not exceed 1,200 r, fractionated over three days.

The series that was irradiated, largely according to the aforegoing principles, does not show any pronounced untoward changes due to radiation either of an early or late nature. This even applies to those cases in which the maximum permitted doses were given. One case,

however, in which the maximum dose was considerably exceeded, testifies to the risk attending such a procedure.

The patient received an 'average dose' of radium amounting to about 1,800 r to the penis from the dorsal side, and some improvement followed. Thirteen months later, roentgen treatment was given in a dose of 2 × 250 r to each of the lateral surfaces, the result being a further improvement. However, permanent, relatively severe changes due to radiation occurred in the penile skin, and on one occasion a sore developed in connection with coitus.

In collaboration with Mr. R. WALSTAM at the Institute of Radiophysics, Stockholm, I measured, during an application of radium, the dose in the testicles. When the radium had been applied, the penis, as is nowadays customary, was fixed against the abdominal skin, which had already been protected by four millimeters of lead. A further lead shield of similar thickness had already been placed against the scrotum, which had been drawn down in the anal direction. Thirty radium tubes, applied in two rows — *i. e.* the largest applicator used — were employed. It was found that with an 'average dose' of 1,100 r the dose in the testicles amounts to about 10 r. Hence fertility is scarcely likely to be affected by radium treatment. In view, however, of the possible risk of damage to the germ plasm it is advisable to reserve radium therapy for those patients who no longer desire offspring; in other cases, roentgen treatment should be resorted to. For if, in this latter therapy, the primary beam should need to pass through the testicles at all, the dose which it produces may be reduced to the requisite degree by means of lead placed between penis and scrotum. Thus, with a roentgen dose of 1,000 r to the penile skin, the dose produced in the testicles by direct radiation will, with a suitably applied shield corresponding to four millimeters of lead, be 0.02 r at the highest. If the shield is expertly fitted, the testicles are not likely to receive any appreciable radiation over and above that amount.

The Radiumhemmet series of cases of plastic induration of the penis for the period 1940 to 1951 comprises one hundred and eighty-eight patients. Fifty-three of these either did not undergo radiation treatment at all or were irradiated according to principles fundamentally differing from those used today; for these reasons, they are not reported here. A further thirty-nine cases have been excluded because they have been followed up for less than six months after the radiation therapy. The age incidence in the remaining series of ninety-six cases will be seen from Diagram 1.

Not all of these cases were examined as uniformly and in such detail as those treated with vitamin E. However, I have found it possible to grade the therapeutic results according to the system described earlier. Of the irradiated cases (seventy-nine treated by the radium method,

though with roentgen rays for the supplementary treatment in the majority of those that underwent such treatment, together with seventeen treated by the roentgen method), nineteen showed 'pronounced improvement' and thirty-four 'moderate improvement' while the other forty-three showed 'poor result'.

Discussion

NIKOLOWSKI, on the basis of the literature and his personal cases, points out that both radiation and vitamin E treatment produce a marked improvement or full healing in about one-fourth, and some improvement in a further number of cases. My experience on the whole accords with his conclusions. Spontaneous improvements occur, it is true; but that fact could scarcely account for the above-mentioned results. Thus BURFORD, in a series of nineteen untreated cases, was able to find spontaneous improvement, evidently of moderate degree, in one case only.

It has not been possible to correlate the therapeutic effect of radium, of roentgen rays or of vitamin E to the patients' age or to the duration or severity of the symptoms. It would thus seem impracticable to choose between the therapeutic methods with respect to the nature of the case. But on the other hand, in the present series there is some evidence that vitamin E may bring about a further improvement in previously irradiated cases, and vice versa. AURIG and SÜSSE have the same experience. In the present state of affairs, therefore, it seems most fitting to treat each new case according to both methods.

I have now found that with each of them the effect may not set in for several months, but then may nevertheless be good. Hence, vitamin E treatment should be continued for four months even if there is no appreciable effect. If a definite effect is obtained, the administration should be maintained as long as distinctly progressive improvement can be observed. Concurrent use of the two therapeutic methods may accordingly make it difficult to assess how long the treatment with vitamin E should be continued. It is advisable, therefore, always to start with the speedier and cheaper irradiation method, and then, unless a very pronounced improvement has occurred, to institute vitamin E treatment after some months. Some time after the end of the latter, supplementary irradiation, if required, may be given in the conventional manner. AURIG and SÜSSE, who also recommend a combination of the two methods, consider that irradiation is more effective after vitamin E treatment; this is based upon the theory that the vitamin causes tissue vascularization, with better requisites for a favourable response to irradiation.

There should be justification to expect that with treatment consistently carried through in accordance with the above principles, the therapeutic results would be further improved.

Supplementary

Dupuytren's contracture, a disease of the palmar aponeurosis producing contracture of the fingers, often coexists with Peyronie's disease, and the two appear to be associated in some way. In 1946, STEINBERG tried vitamin E in Dupuytren's contracture, and in two papers he has reported fairly good results. SCOTT and SCARDINO (11), THOMSON, and KIRK and CHIEFFI have communicated similar experiences. LANGSTON and BADRE, PARSONS, and KING, on the other hand, have not observed any objective changes with vitamin E therapy.

At Radiumhemmet, twenty-two non-selected cases of Dupuytren's contracture — three of which are included in the present series of Peyronie's disease cases — have been treated with 300 mg alpha-tocopherol daily for periods varying between four and eleven months. In one case a very slight subjective and objective improvement and in six cases only a certain subjective improvement was observed, while fifteen showed no response. These results scarcely provide an incentive to further use of vitamin E in Dupuytren's contracture, at all events as a single therapeutic agent.

SUMMARY

Following a discussion of the surgical method of treatment, the non-surgical methods (roentgen and radium irradiation and administration of vitamin E) are described and critically appraised on the basis of Radiumhemmet's series and of the available literature. A description is given of the dosimetric investigations that were carried out respecting the irradiation methods. General principles are presented for combined irradiation and vitamin E therapy. Administration of vitamin E has also been tried in Dupuytren's contracture and the value of the method in this disease is discussed.

ZUSAMMENFASSUNG

Im Anschluss an die Diskussion der chirurgischen Behandlungsmethoden werden die übrigen Methoden (Röntgen- und Radiumbehandlung sowie Administrierung von Vitamin E) beschrieben und unter Zugrundelegung des Materials des Radiumhemmet und der zugänglichen Literatur kritisch bewertet. Dosimetrische Untersuchungen, die bezüglich der Strahlenbehandlungsmethoden ausgeführt wurden, werden beschrieben. Allgemeine Richtlinien für eine kombinierte Behandlung mit Bestrahlung und Vitamin E werden angegeben. Vitamin E ist auch in Fällen mit Dupuytrenscher Kontraktur versuchsweise angewendet worden; der Wert der Methode bei dieser Krankheit wird diskutiert.

RÉSUMÉ

Après une étude critique du traitement chirurgical, l'auteur décrit les méthodes non-chirurgicales (roentgen et curiethérapie et administration de vitamine E) et, se basant sur la série du Radiumhemmet et sur la littérature, en détermine de façon critique

la valeur. Il décrit les études dosimétriques effectuées pour chacune des méthodes d'irradiation. Il indique les principes généraux d'irradiation combinée et de traitement par la vitamine E. Il a aussi essayé l'administration de vitamine E dans la maladie de Dupuytren et discute la valeur de ce traitement dans cette affection.

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BOOK REVIEWS

CHANGES IN THE CHEST ROENTGENOGRAM IN BOECK'S SARCOID OF THE LUNGS. A STUDY OF THE COURSE OF THE DISEASE IN 90 CASES. By Lorentz Nitter, 202 pages, 125 illustrations and 14 tables. Acta radiol. Suppl. 105. Stockholm 1953. Swed. Kr. 25. —.

In an effort to classify the roentgenographic pattern in Boeck's sarcoid of the lungs a series of 90 cases as originally observed at the Department of Radiology of the University Hospital of Oslo, have been followed up. The average observation period was $5^1/_2$ years, but a considerable proportion of the cases have been watched for a longer time, some of them up to 15 to 20 years.

The work has primarily been aimed at an elucidation of the various types of pulmonary involvement and their relation to the prognosis from a roentgenographic point of view. Clinical data to confirm the diagnosis, however, have been considered essential, for which reason particular attention has been paid to biopsy studies, Kveim and tuberculin testing, examination of the blood, and the occurrence of concurrent extrapulmonary manifestations.

The clinical findings together with the roentgenographic observations constitute the two main chapters of the work. A detailed report of the individual cases and 125 chest film reproductions have also been included.

Based on the observations as mentioned and a total of 513 chest roentgenograms as available from the cases, 5 types or stages of pulmonary involvement have been distinguished and described in detail.

The hilar lymph nodes are probably the structures affected first (stage I). The subsequent perihilar streaking indicates the spread of the disease into the interstitial tissue of the lungs (stage II). Another highly characteristic finding is paratracheal adenopathy. This was observed in 36 cases and obviously occurs in close connection with the bilateral hilar adenopathy.

While the hilar and contingent paratracheal adenopathy are still persisting, initial parenchymal lesions of either the coarse nodular type of stage III or the miliary type of stage IV may be seen to develop. These types run an entirely different course.

Concerning stages III and IV it will be seen that the prognosis for cases with miliary infiltration of the stage IV type is generally favourable. In the 28 patients presenting this type of lesion, complete regression occurred within 6 months to 3 years in 26 cases.

Stage III, that is, the coarse pulmonary nodulation, always seems to be followed by pulmonary fibrosis affecting the prognosis adversely. Of the 41 patients presenting or having presented this type of lesion, 28 showed evidence of subsequent fibrosis. Observations in a number of cases indicate that the fibrosis resulting from this type of involvement occurs early so as to manifest itself roentgenographically simultaneously with the clearing of the stage III densities. Permanent regression was not observed in any of the patients with this type of lesion.

The further development of fibrosis, stage V, may occasionally be characterized by rapid progression so as to prove fatal within a few years. In most instances, however, the progression is less rapid with a gradual onset of incapacitating symptoms and a duration of illness of up to 20 years. Twelve of the 13 patients who died as a result of their pulmonary disease presented definite fibrosis and about 30 per cent of those with pulmonary fibrosis died while under observation. Another 15 patients with fibrosis but still alive all had serious symptoms. The vast majority of these cases must be presumed to have a poor prognosis.

To summarize, it may be said that the general characteristics of the pulmonary changes are their bilateral, symmetrical distribution and the great variation of the roentgenographic appearances over a period of several years. The signs are usually so characteristic that the roentgen findings alone will be highly suggestive.

In 68 patients, biopsy specimens were taken from sites other than the lungs, preferably from skin and lymph nodes. A total of 125 microscopic sections were examined. Birefringent foreign bodies were demonstrated in but 7 of the patients with positive biopsies. The histopathologic findings are specified in a general table.

Kveim and tuberculin tests were performed in all the patients. Carried out in the presence of a recent bilateral hilar adenopathy, Kveim's test seems to be of great diagnostic value. A positive response was thus obtained in 95 per cent of the cases with this type of involvement, that is, stage II lesions. Performed at a later stage the test is of far less value. An analysis of the cases in which Kveim's test was negative indicates failure of the test in approximately 15 per cent.

Tuberculin tests were negative in 69 patients or 76 per cent. In 21 patients who were reactors to tuberculin at the initial examination or previously, tuberculin positivity persisted in only 6 cases while waning or reversed reactions were observed in 15 patients. In 7 of these patients, reconversion occurred after clearing of the parenchymal lesions.

The blood sedimentation rate was normal in 24 patients many of whom had severe pulmonary involvement. Reversion of the albumin-globulin ratio was observed in a large proportion of cases.

Extrapulmonary manifestations were observed in 67 patients. Only 25 presented clinical evidence of pulmonary involvement at the initial examination. In 20 patients the pulmonary disease was detected incidentally on mass chest survey or other routine examinations. The remaining cases had sought medical advice because of other manifestations, such as skin lesions, peripheral lymphadenopathy, eye lesions, parotitis, etc.

Problems concerning the etiology of the disease do not fall within the scope of this study. The etiology has mainly been considered on the basis of the roentgenographic and patho-anatomic findings and clinical observations.

The true incidence of Boeck's sarcoid of the lungs is no doubt considerably greater than that actually observed in roentgenographic practice. The finding of bilateral hilar adenopathy, with or without associated enlargement of the paratracheal nodes in an apparently healthy individual, should always be considered an indication for further control. A large number of such cases are probably being diagnosed but not watched because of the absence of clinical symptoms.

Autoreview.

DIE TELERÖNTGENTHERAPIE. Von W. Teschendorf: 72 Seiten, 8 Abbildungen. George Thieme Verlag. Stuttgart, 1953, D.M. 8.70.

TESCHENDORF has now had twenty years experience of general irradiation with small doses of roentgen. General irradiation is nowadays mostly indicated in the leukemias, although treatment with P^{32} is the method of choice in polycythemia.

General treatment with roentgen may be interrupted if the blood values should show a tendency to fall too violently. On the other hand, in carrying out treatment with radio-active isotopes, disagreeable surprises and possibly aplastic anaemia may be encountered by reason of the fact that this form of therapy cannot be broken off in the same way as is possible with roentgen. TESCHENDORF lays down minimum limits of 100,000 for the thrombocytes and 2,000 for the whites in general irradiation. It is worthwhile following the prothrombin value; it should remain constant during the treatment.

TESCHENDORF gives 3—5 r in the leukemias and treatment every three to four days. The dose is divided each time between the front and the back of the body. The eyes as well

as the genitalia are always protected. Lowering of the white cells to below 20,000 is not aimed at. The determining factors as regards the treatment and its duration are the general condition of the patient and his capacity for work. The author does not appear to investigate the basal metabolism; if treatment is to be given, its rate is of great value for the assessment.

TESCHENDORF does not administer general irradiation these days in malignant lymphogranulomatosis excepting in certain cases, for example, if the S. R. rises but there is no enlargement of the lymph glands. He points out that Sternberg disease often runs a more favourable and slower course in women than in men and consequently suggests the trial treatment of men by female hormones concurrently with the roentgen treatment.

In many cases of disseminated cancer metastases the author has seen good effects with general irradiation of 25—50 r and five treatments a week with a total of up to fifty treatments in all.

Experiments in the pneumonias and pulmonary tuberculosis show that general irradiation in doses of 3 r per week has a beneficial and stimulating effect upon the reticulo-endothelial system with improvement of the blood values and raising of the power of resistance.

The book is readable, concise and well worth perusing.

Folke Jacobsson.

THE RADIOLOGY OF BONES AND JOINTS. (AN INTRODUCTION TO THE STUDY OF TUMOURS AND OTHER DISEASES OF BONE.) By James F. Brailsford. 875 pages, 600 illustrations. J. & A. Churchill Limited, London 1953. 90 shillings.

This monograph, the work of one man, is an impressive achievement. The book, as in previous editions, is divided into two parts. In the special part, the bony skeleton and the joints are dealt with regionally from the aspect of pathologic changes. The arrangement is reversed in the general section in which the different disturbances of growth, deformities, diseases and tumours are considered as entities and their appearances and character in the various regions of the bony skeleton discussed.

The descriptions are based upon the author's great personal experience and practically all the roentgenograms are derived from his own material. In one place, his big-toe joint serves as an example of osteo-arthritis. The diagnoses in the cases reported are founded upon pathologo-anatomic examinations or definite clinical findings. The author's prolonged observations of individual cases has enabled him to give instructive descriptions of the course of the pathologic changes. The picture material is generally excellent both as regards quality and selection.

In those instances where the author's own material and experience do not suffice, reference is made to the available literature. He has by these additions succeeded in producing an extensive monograph.

The chapter on the skull is of value as part of the survey of the skeleton in systemic diseases but fills no claim as being complete so far as cerebral diagnosis is concerned.

The author erroneously maintains the old notion of persisting epiphyses of the vertebral bodies. He regards fragmentation of the apophysis of the os calcis as a pathologic condition and the cause of pain. For the sake of personal prestige, he argues against the conception of 'osteoid-osteoma'.

This magnificent work has its obviously distinguished place in the roentgenologic literature. To the realm of such difficult and extensive diagnostics as those of the skeleton, it forms a valuable means of access by reason of the copious case-histories as well as the diagnostic information rendered possible by its monographic nature.

Folke Knutsson.